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(54) **Title:** METHOD OF DESIGNING AGONISTS AND ANTAGONISTS TO IGF RECEPTOR

(57) **Abstract**

The present invention relates to a method of designing compounds able to bind to a molecule of the insulin receptor family and to modulate the activity mediated by the receptor based on the 3–D structure coordinates of a IGF–1 receptor crystal of Figure 1.

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METHOD OF DESIGNING AGONISTS AND ANTAGONISTS TO IGF RECEPTOR

Field of the Invention

This invention relates to the field of receptor structure and receptor/ligand interactions. In particular it relates to the field of using receptor structure to predict the structure of related receptors and to the use of the determined structures and predicted structures to select and screen for agonists and antagonists of the polypeptide ligands.

Background of the Invention

Insulin is the peptide hormone that regulates glucose uptake and metabolism. The two types of diabetes mellitus, are associated either with an inability to produce insulin because of destruction of the pancreatic islet cells (Homo-Delarche, F. & Boitard, C.,1996, Immunol. Today 10: 456-460) or with poor glucose metabolism resulting from either insulin resistance at the target tissues, or from inadequate insulin secretion by the islets or faulty liver function (Taylor, S. I., et al., 1994, Diabetes, 43: 735-740).

Insulin-like growth factors-1 and 2 (IGF-1 and 2) are structurally related to insulin, but are more important in tissue growth and development than in metabolism. They are primarily produced in the liver in response to growth hormone, but are also produced in most other tissues, where they function as paracrine/autocrine regulators. The IGFs are strong mitogens, and are involved in numerous physiological states and certain cancers (Baserga, R., 1996, TibTech 14: 150-152).

Epidermal growth factor (EGF) is a small polypeptide cytokine that is unrelated to the insulin/IGF family. It stimulates marked proliferation of epithelial tissues, and is a member of a larger family of structurally-related cytokines, such as transforming growth factor α, amphiregulin, betacellulin, heparin-binding EGF and some viral gene products. Abnormal EGF family signalling is a characteristic of certain cancers (Soler, C. & Carpenter, G., 1994 In Nicola, N. (ed) Guidebook to Cytokines and Their receptors", Oxford Univ. Press, Oxford, pp194-197; Walker, F. & Burgess, A. W., 1994, In Nicola, N. (ed) Guidebook to Cytokines and Their receptors", Oxford Univ. Press, Oxford, pp198-201).

Each of these growth factors mediates its biological actions through binding to the corresponding receptor. The IR, IGF-1R and the insulin receptor-related receptor (IRR), for which the ligand is not known, are closely related to each other, and are referred to as the insulin receptor subfamily. A

large body of information is now available concerning the primary structure of these insulin receptor subfamily members (Ebina, Y., et al., 1985 Cell 40: 747-758; Ullrich, A., et al., 1985, Nature 313: 756-761; Ullrich, A. et al., 1986, EMBO J 5: 2503-2512; Shier, P. & Watt, V. M., 1989, J. Biol. Chem. 264: 14605-14608) and the identification of some of their functional domains (for reviews see De Meyts, P. 1994, Diabetologia 37: 135-148; Lee, J. & Pilch, P. F. 1994 Amer. J. Physiol. 266: C319-C334.; Schaffer, L. 1994, Eur. J. Biochem. 221: 1127-1132). IGF-1R, IR and IRR are members of the tyrosine kinase receptor superfamily and are closely related to the epidermal growth factor receptor (EGFR) subfamily, with which they share significant sequence identity in the extracellular region as well as in the cytoplasmic kinase domains (Ullrich, A. et al., 1984 Nature 309: 418-425; Ward, C. W. et al., 1995 Proteins: Structure Function & Genetics 22: 141-153). Both the insulin and EGF receptor subfamilies have a similar arrangement of two homologous domains (L1 and L2) separated by a cys-rich region of approximately 160 amino acids containing 22-24 cys residues (Bajaj, M., et al., 1987 Biochim. Biophys. Acta 916: 220-226; Ward, C. W. et al., 1995 Proteins: Structure Function & Genetics 22: 141-153). The C-terminal portion of the IGF-1R ectodomain (residues 463 to 906) is comprised of four domains: a connecting domain, two fibronectin type 3 (Fn3) repeats, and an insert domain (O'Bryan, J. P., et al., 1991 Mol Cell Biol 11: 5016-5031). The C-terminal portion of the EGFR ectodomain (residues 477-621) consists solely of a second cys-rich region containing 20 cys residues (Ullrich, A. et al., 1984, Nature 309: 418-425).

Little is known about the secondary, tertiary and quaternary structure of the ectodomains of these receptor subfamilies. Unlike the members of the EGFR subfamily which are transmembrane monomers which dimerise on binding ligand, the IR subfamily members are homodimers, held together by disulphide bonds. The extracellular region of the IR/IGF-1R/IRR monomers contains an α-chain (~ 703 to 735 amino acid residues) and 192-196 residues of the ß-chain. There is a ~23 residue transmembrane segment, followed by the cytoplasmic portion (354 to 408 amino acids), which contains the catalytic tyrosine kinase domain flanked by juxtamembrane and C-tail regulatory regions and is responsible for mediating all receptor-specific functions (White, M. F. & Kahn, C. R. 1994 J. Biol. Chem. 269: 1-4). Chemical analyses of the receptor suggest that the α-chains are linked to the ß-chains

via a single disulphide bond, with the IR dimer being formed by at least two α-α disulphide linkages (Finn, F. M., et al., 1990, Proc. Natl. Acad. Sci. 87: 419-423; Chiacchia, K. B., 1991, Biochem. Biophys. Res. Commun. 176, 1178-1182; Schaffer, L. & Ljungqvist, L., 1992, Biochem. Biophys. Res. Comm. 189: 650-653; Sparrow, L. G., et al., 1997, J. Biol. Chem. 47: 29460-29467).

Although the three-dimensional (3D) structures of the ligands EGF, TGF-alpha (Hommel, U., et al., 1992, J. Mol. Biol. 227:271-282), insulin (Dodson, E. J., et al., 1983, Biopolymers 22:281-291), IGF-1 (Sato, A., et al., 1993, Int J Peptide Protein Res 41:433-440) and IGF-2 (Torres, A. M., et al.,1995, J. Mol. Biol. 248:385-401) are known, and numerous analytical and functional studies of ligand binding to EGFR (Soler, C. & Carpenter, G., 1994 In Nicola (ed) Guidebook to Cytokines and Their receptors", Oxford Univ. Press, Oxford, pp194-197), IGF-1R and IR (see De Meyts, P., 1994 Diabetologia, 37:135-148) have been carried out, the mechanisms of ligand binding and subsequent transmembrane signalling have not been resolved.

Ligand-induced, receptor-mediated phosphorylation is the signalling mechanism by which most cytokines, polypeptide hormones and membrane-anchored ligands exert their biological effects. The primary kinase may be part of the intracellular portion of the transmembrane receptor protein, as in the tyrosine kinase receptors (for review see Yarden, Y., et al., 1988, Ann. Rev. Biochem. 57:443-478) or the Ser/Thr kinase receptors (Alevizopoulos, A. & Mermod, N., 1997, BioEssays, 19:581-591) or may be non-covalently associated with the cytoplasmic tail of the transmembrane protein(s) making up the receptor complex, as in the case of the haemopoietic growth factor receptors (Stahl, N., et al., 1995, Science 267:1349-1353). The end result is the same, ligand binding leads to receptor dimerization or oligomerization or a conformational change in pre-existing receptor dimers or oligomers, resulting in activation by transphosphorylation, of the covalently attached or non-covalently associated protein kinase domains (Hunter, T., 1995, Cell, 80:225-236).

Many oncogenes have been shown to be homologous to growth factors, growth factor receptors or molecules in the signal transduction pathways (Baserga, R.,1994 Cell, 79:927-930; Hunter, T., 1997 Cell, 88:333-346). One of the best examples is v-Erb (related to the EGFR). Since overexpression of a number of growth factor receptors results in ligand-dependent transformation, an alternate strategy for oncogenes is to regulate

the expression of growth factor receptors or their ligands or to directly bind to the receptors to stimulate the same effect (Baserga, R., 1994 Cell, 79:927-930). Examples are v-Src, which activates IGF-1 R intracellularly; c-Myb, which transforms cells by enhancing the expression of IGF1R; and SV40 T antigen which interacts with the IGF-1R and enhances the secretion of IGF-1 (see Baserga, R.,1994 Cell, 79:927-930 for review). Cells in which the IGF-1R has been disrupted or deleted cannot be transformed by SV40 T antigen. If oncogenes activate growth factors and their receptors, then tumour suppressor genes should have the opposite effect. One good example of this is the Wilm's tumour suppressor gene, WT1, which suppresses the expression of IGF-1R (Drummond, J. A., et al., 1992, Science, 257:275-277). Cells that are driven to proliferate by oncogenes undergo massive apoptosis when growth factor receptors are ablated, since, unlike normal cells, they appear unable to withdraw from the cell-cycle and enter into the G_0 phase (Baserga, R.,1994 Cell, 79:927-930).

The insulin-like growth factor-1 receptor (IGF-1R) is one of several growth-factor receptors that regulate the proliferation of mammalian cells. However, its ubiquitousness and certain unique aspects of its function make IGF-1R an ideal target for specific therapeutic interventions against abnormal growth, with very little effect on normal cells (see Baserga, R., 1996 TIBTECH, 14:150-152). The receptor is activated by IGF1, IGF2 and insulin, and plays a major role in cellular proliferation in at least three ways: it is essential for optimal growth of cells *in vitro* and *in vivo*; several cell types require IGF-1R to maintain the transformed state; and activated IGF-1R has a protective effect against apoptotic cell death (Baserga, R., 1996 TIBTECH, 14:150-152). These properties alone make it an ideal target for therapeutic interventions. Transgenic experiments have shown that IGF-1R is not an absolute requirement for cell growth, but is essential for the establishment of the transformed state (Baserga, R.,1994 Cell, 79: 927-930). In several cases (human glioblastoma, human melanoma; human breast carcinoma; human lung carcinoma; human ovarian carcinoma; human rhabdomyosarcoma; mouse melanoma, mouse leukaemia; rat glioblastoma; rat rhabdomyosarcoma; hamster mesothelioma) the transformed phenotype can be reversed by decreasing the expression of IGF-1R using antisense to IGF-1R (Baserga, R., 1996 TIBTECH 14:150-152); or by interfering with its function by antibodies to IGF-1R (human breast carcinoma; human

rhabdomyosarcoma) or by dominant negatives of IGF-1R (rat glioblastoma; Baserga, R.,1996 TIBTECH 14:150-152).

Three effects are observed when the function of IGF-1R is impaired: tumour cells undergo massive apoptosis which results in inhibition of tumourogenesis; surviving tumour cells are eliminated by a specific immune response; and such a host response can cause a regression of an established wild-type tumour (Resnicoff, M., et al., 1995, Cancer Res. 54:2218-2222). These effects, plus the fact that interference with IGF-1R function has a limited effect on normal cells (partial inhibition of growth without apoptosis) makes IGF-1R a unique target for therapeutic interventions (Baserga, R., 1996 TIBTECH 14:150-152). In addition IGF-1R is downstream of many other growth factor receptors, which makes it an even more generalised target. The implication of these findings is that if the number of IGF-1Rs on cells can be decreased or their function antagonised, then tumours cease to grow and can be removed immunologically. These studies establish that IGF-1R antagonists will be extremely important therapeutically.

Many cancer cells have constitutively active EGFR (Sandgreen, E. P., et al., 1990, Cell, 61:1121-135; Karnes, W. E. J., et al., 1992, Gastroenterology, 102:474-485) or other EGFR family members (Hines, N. E.,1993, Semin. Cancer Biol. 4:19-26). Elevated levels of activated EGFR occur in bladder, breast, lung and brain tumours (Harris, A. L., et al., 1989, In Furth & Greaves (eds) The Molecular Diagnostics of human cancer. Cold Spring Harbor Lab. Press, CSH, NY, pp353-357). Antibodies to EGFR can inhibit ligand activation of EGFR (Sato, J. D., et al., 1983 Mol. Biol. Med. 1:511-529) and the growth of many epithelial cell lines (Aboud-Pirak E., et al., 1988, J. Natl Cancer Inst. 85:1327-1331). Patients receiving repeated doses of a humanised chimeric anti-EGFR monoclonal antibody showed signs of disease stabilization. The large doses required and the cost of production of humanised monoclonal antibody is likely to limit the application of this type of therapy. These findings indicate that the development of EGF antagonists will be attractive anticancer agents.

Summary of the Invention

The present inventors have now obtained 3D structural information concerning the insulin-like growth factor receptor (IGF-1R). This information can be used to predict the structure of related members of the insulin

receptor family and provides a rational basis for the development of ligands for specific therapeutic applications.

Accordingly, in a first aspect the present invention provides a method of designing a compound able to bind to a molecule of the insulin receptor family and to modulate an activity mediated by the molecule, including the step of assessing the stereochemical complementarity between the compound and the receptor site of the molecule, wherein the receptor site includes:

(a) amino acids 1 to 462 of the receptor for IGF-1, having the atomic coordinates substantially as shown in Figure 1;

(b) a subset of said amino acids, or;

(c) amino acids present in the amino acid sequence of a member of the insulin receptor family, which form an equivalent three-dimensional structure to that of the receptor molecule as depicted in Figure 1.

The phrase "insulin receptor family" encompasses, for example, IGF-1R, IR and IRR. In general, insulin receptor family members show similar domain arrangements and share significant sequence identity (preferably at least 40% identity).

By "stereochemical complementarity" we mean that the biologically active substance or a portion thereof correlates, in the manner of the classic "lock-and-key" visualisation of ligand-receptor interaction, with the groove in the receptor site.

In a preferred embodiment of this aspect of the invention, the compound is selected or modified from a known compound identified from a database.

In a further preferred embodiment, the compound is designed so as to complement the structure of the receptor molecule as depicted in Figure 1.

In a further preferred embodiment, the compound has structural regions able to make close contact with amino acid residues at the surface of the receptor site lining the groove, as depicted in Figure 2.

In a further preferred embodiment, the compound has a stereochemistry such that it can interact with both the L1 and L2 domains of the receptor site.

In a further preferred embodiment, the compound has a stereochemistry such that it can interact with the L1 domain of a first monomer of the receptor homodimer, and with the L2 domain of the other monomer of the receptor homodimer.

In a further preferred embodiment, the interaction of the compound with the receptor site alters the position of at least one of the L1, L2 or cysteine-

rich domains of the receptor molecule relative to the position of at least one of the other of said domains. Preferably, the compound interacts with the β sheet of the L1 domain of the receptor molecule, thereby causing an alteration in the position of the L1 domain relative to the position of the cysteine-rich domain or of the L2 domain. Alternatively, the compound interacts with the receptor site in the region of the interface between the L1 domain an the cysteine-rich domain of the receptor molecule, thereby causing the L1 domain and the cysteine-rich domain to move away from each other. In another preferred embodiment, the compound interacts with the hinge region between the L2 domain and the cysteine-rich domain of the receptor molecule, thereby causing an alteration in the positions of the L2 domain and the cysteine-rich domain relative to each other.

In a further preferred embodiment, the stereochemical complementarity between the compound and the receptor site is such that the compound has a K_b for the receptor side of less than 10^{-6}M, more preferably is less than 10^{-8}M.

In a further preferred embodiment or the first aspect of the present invention, the compound has the ability to increase an activity mediated by the receptor molecule.

In a further preferred embodiment, the compound has the ability to decrease an activity mediated by the receptor molecule. Preferably, the stereochemical interaction between the compound and the receptor site is adapted to prevent the binding of a natural ligand of the receptor molecule to the receptor site. It is preferred that the compound has a K_1 of less than 10^{-6}M, more preferably less than 10^{-8}M and more preferably less than 10^{-9}M.

In a further preferred embodiment of the first aspect of the present invention, the receptor is the IGF-1R, or the insulin receptor.

In a second aspect, the present invention provides a computer-assisted method for identifying potential compounds able to bind to a molecule of the insulin receptor family and to modulate an activity mediated by the molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data comprising the atomic coordinates of the IGF-1R molecule as shown in Figure 1, or a subset thereof;

(b) generating, using computer methods, a set of atomic coordinates of a structure that possesses stereochemical complementarity to the atomic

coordinates of the IGF-1R site as shown in Figure 1, or a subset thereof, thereby generating a criteria data set;

(c) comparing, using the processor, the criteria data set to a computer database of chemical structures;

(d) selecting from the database, using computer methods, chemical structures which are structurally similar to a portion of said criteria data set; and

(e) outputting, to the output device, the selected chemical structures which are similar to a portion of the criteria data set.

In a preferred embodiment of the second aspect, the programmed computer includes a data storage system which includes the dtatbase of chemical structures.

In a preferred embodiment of the second aspect, the method is used to identify potential compounds which have the ability to decrease an activity mediated by the receptor.

In another preferred embodiment, the computer-assisted method further includes the step of selecting one or more chemical structures from step (e) which interact with the receptor site of the molecule in a manner which prevents the binding of natural ligands to the receptor site.

In another preferred embodiment, the computer-assisted method further includes the step of obtaining a compound with a chemical structure selected in steps (d) and (e), and testing the compound for the ability to decrease an activity mediated by the receptor.

In a further preferred embodiment, the computer-assisted method is used to identify potential compounds which have the ability to increase an activity mediated by the receptor molecule.

In another preferred embodiment, the computer-assisted method further includes the step of obtaining a molecule with a chemical structure selected in steps (d) and (e), and testing the compound for the ability to increase an activity mediated by the receptor.

In a further preferred embodiment of the second aspect of the present invention, the receptor is the IGF-1R, or the insulin receptor.

In a third aspect, the present invention provides a method of screening of a putative compound having the ability to modulate the activity of a receptor of the insulin receptor family, including the steps of identifying a putative compound by a method according to the first or second aspects, and testing the

compound for the ability to increase or decrease an activity mediated by the receptor.

In a preferred embodiment of the third aspect, the test is carried out *in vitro*.

In a further preferred embodiment of the third aspect, the test is a high throughput assay.

In a preferred embodiment of the third aspect, the test is carried out *in vivo*.

Brief Description of the Drawings

Figure 1. IGF-1R residues 1-462, in terms of atomic coordinates refined to a resolution of 2.6 Å (average accuracy ≈ 0.3Å). The coordinates are in relation to a Cartesian system of orthogonal axes.

Figure 2. Depiction of the residues lining the groove of the IGF-1R receptor fragment 1-462.

Figure 3. Gel filtration chromatography of affinity-purified IGF-1R/462 protein. The protein was purified on a Superdex S200 column (Pharmacia) fitted to a BioLogic L.C. system (Biorad), equilibrated and eluted at 0.8 ml/min with 40 mM Tris/150 mM NaCl/0.02% NaN3 adjusted to pH 8.0. (a) Protein eluting in peak 1 contained aggregated IGF-1R/462 protein, peak 2 contained monomeric protein and peak 3 contained the c-myc undecapeptide used for elution from the Mab 9E10 immunoaffinity column. (b) Non-reduced SDS-PAGE of fraction 2 from IGF-1R/462 obtained following Superdex S200 (Fig.1a). Standard proteins are indicated.

Figure 4. Ion exchange chromatography of affinity-purified, truncated IGF-1R ectodomain. A mixture of gradient and isocratic elution chromatography was performed on a Resource Q column (Pharmacia) fitted to a BioLogic System (Biorad), using 20 mM Tris/pH 8.0 as buffer A and the same buffer containing 1M NaCl as buffer B. Protein solution in TBSA was diluted at least 1:2 with water and loaded onto the column at 2 ml/min. Elution was monitored by absorbance (280 nm) and conductivity (mS/cm). Target protein (peak 2) eluted isocratically with 20 mM Tris/0.14 M NaCl pH 8.0. Inset:

Isoelectric focusing gel (pH 3 - 7; Novex Australia Pty Ltd)of fraction 2. The pI was estimated at 5.1 from standard proteins (not shown).

Figure 5. Polypeptide fold for residues 1-462 of IGF-1R. The L1 domain is at the top, viewed from the N-terminal end and L2 is at the bottom. The space at the centre is of sufficient size to accommodate IGF-1. Helices are indicated by curled ribbon and b-strands by arrows. Cysteine side chains are drawn as ball-and-stick with lines showing disulfide bonds. The arrow points in the direction of view for L1 in Figure 7.

Figure 6. Amino acid sequences of IGF-1R and related proteins. a, L1 and L2 domains of human IGF-1R and IR are shown based on a sequence alignment for the two proteins and a structural alignment for the L1 and L2domains. Positions showing conservation physico-chemical properties of amino acids are boxed, residues used in the structural alignment are shown in Times Italic and residues which form the Trp 176 pocket are in Times Bold. Secondary structure elements for L1 (above the sequences) and L2 (below) are indicated as cylinders for helices and arrows for β-strands. Strands are shaded (pale, medium and dark grey) according to the β-sheet to which they belong. Disulfide bonds are also indicated. b, Cys-rich domains of human IGF-1R, IR and EGFR (domains 2 and 4) are aligned based on sequence and structural considerations. Secondary structural elements and disulfide bonds are indicated above the sequences. The dashed bond is only present in IR. Different types of disulfide bonded modules are labelled below the sequences as open, filled or broken lines. Boxed residues show conservation of physico-chemical properties and structurally conserved residues for modules 4-7 are shown in Times Italic. Residues from EGFR which do not conform to the pattern are in lowercase with probable disulfide bonding indicated below and the conserved Trp 176 and the semi-conserved Gln 182 are in Times Bold.

Figure 7. Stereo view of a superposition of the L1 (white) and L2 (black) domains. Residues numbers above are for L1 and below for L2. The side chain of Trp 176 which protrudes into the core of L1 is drawn as ball-and-stick.

Figure 8. Schematic diagram showing the association of three β-finger motifs. β-strands are drawn as arrows and disulfide bonds as zigzags.

Figure 9: Sequence alignment of hIGF-1R, hIR and hIRR ectodomains, derived by use of the PileUp program in the software package of the Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA.
For assignment of homologous 3D structures see Figure 6.

Figure 10 Gel filtration chromatography of insulin receptor ectodomain and MFab complexes. hIR -11 ectodomain dimer (5 - 20 mg) was complexed with MFab derivatives (15-25 mg each) of the anti-hIR antibodies 18-44, 83-7 and 83-14 (Soos et al., 1986). Flution profiles were generated from samples loaded on to a Superdex S200 column (Pharmacia), connected to a BioLogic chromatography system (Biorad) and monitored at 280 nm. The column was eluted at 0.8 ml/min with 40 mM Tris/150 mM sodium chloride/0.02% sodium azide buffer adjusted to pH 8.0: Profile 0, hIR -11 ectodomain, Profile 1, ectodomain mixed with MFab 18-44; Profile 2 , ectodomain mixed with MFab18-44 and MFab 83-14; Profile 3, ectodomain mixed with MFab 18-44, MFab 83-14 and MFab 83-7. The apparent mass of each complex was determined from a plot of the following standard proteins: thyroglobulin (660 kDa), ferritin (440 kDa), bovine gamma globulin (158 kDa), bovine serum albumin (67 kDa), chicken ovalbumin (44 kDa) and equine myoglobin (17 kDa).

Figure 11 Schematic representations of electron microscopy images of the hIR ectodomain dimer.

Detailed Description of the Invention

We describe herein the expression, purification, and crystallization of a recombinant truncated IGF-1R fragment (residues 1-462) containing the L1-cysteine-rich-L2 region of the ectodomain. The selected truncation position is just downstream of the exon 6/exon 7 junction (Abbott, A. M., et al., 1992. J Biol Chem., 267:10759-10763), and occurs at a position where the sequences of the IR and EGFR families diverge markedly (Ward, C. W., et al.,1995, Proteins: Struct., Funct., Genet. 22:141-153; Lax, I., et al., 1988, Molec. Cellul. Biol. 8:1970-1978) suggesting it represents a domain boundary. To

limit the effects of glycosylation, the IGF-1R fragment was expressed in Lec8 cells, a glycosylation mutant of Chinese hamster ovary (CHO) cells, whose defined glycosylation defect produces N-linked oligosaccharides truncated at N-acetyl glucosamine residues distal to mannose residues (Stanley, P. 1989, Molec. Cellul. Biol. 9:377-383). Such an approach has facilitated glycoprotein crystallization (Davis, S. J., et al., 1993, Protein Eng. 6:229-232; Liu, J., et al., 1996, J. Biol. Chem. 271:33639-33646).

The IGF-1R construct described herein includes a c-myc peptide tag (Hoogenboom, H. R., et al.,1991, Nucleic Acids Res. 19:4133-4137) that is recognised by the Mab 9E10 (Evan, G. I., et al., 1985, Mol. Cell. Biol. 5:3610-3616) enabling the expressed product to be purified by peptide elution from an antibody affinity column followed by gel filtration over Superdex S200. The purified proteins crystallized under a sparse matrix screen (Jancarik, J. & Kim, S.-H., 1991, J. Appl. Cryst. 24:409-411) but the crystals were of variable quality, with the best diffracting to 3.0-3.5Å. Isocratic gradient elution by anion-exchange chromatography yielded protein that was less heterogenous and gave crystals of sufficient quality to determine the structure of the first three domains of the human IGF-1R.

The IGF-1R fragment consisted of residues 1-462 of IGF-1R linked via an enterokinase-cleavable pentapeptide sequence to an eleven residue c-myc peptide tag at the C-terminal end. The fragment was expressed in Lec8 cells by continuous media perfusion in a bioreactor using porous carrier disks. It was secreted into the culture medium and purified by peptide elution from an anti-c-myc antibody column followed by Superdex S200 gel filtration. The receptor fragment bound two anti-IGF-1R monoclonal antibodies, 24-31 and 24-60, which recognize conformational epitopes, but could not be shown to bind IGF-1 or IGF-2. Crystals of variable quality were grown as rhombic prisms in 1.7 M ammonium sulfate at pH 7.5 with the best diffracting to 3.0-3.5 Å. Further purification by isocratic elution on an anion-exchange column gave protein which produced better quality crystals, diffracting to 2.6 Å, that were suitable for X-ray structure determination.

The structure of this fragment (IGF-1R residues 1-462; L1-cys rich-L2 domains) has been determined to 2.6 Å resolution by X-ray diffraction. The L domains each adopt a compact shape consisting of a single stranded right-handed β-helix. The cys-rich region is composed of eight disulphide-bonded modules, seven of which form a rod-shaped domain with modules associated

in a novel manner. At the centre of this reasonably extended structure is a space, bounded by all three domains, and of sufficient size to accommodate a ligand molecule. Functional studies on IGF-1R and other members of the insulin receptor family show that the regions primarily responsible for hormone-binding map to this central site. Thus this structure gives a first view of how members of the insulin receptor family might interact with their ligands.

Another group has reported the crystallization of a related receptor, the EGFR, in a complex with its ligand EGF (Weber, W., et al., 1994, J Chromat. 679:181-189). However, difficulties were encountered with these crystals which diffracted to only 6 Å, insufficient for the determination of an atomic resolution structure of this complex (Weber, W., et al., 1994, J Chromat 679:181-189) or the generation of accurate models of structurally related receptor domains such as IGF-1R and IR by homology modelling.

The present inventors have developed 3D structural information about cytokine receptors in order to enable a more accurate understanding of how the binding of ligand leads to signal transduction. Such information provides a rational basis for the development of ligands for specific therapeutic applications, something that heretofore could not have been predicted *de novo* from available sequence data.

The precise mechanisms underlying the binding of agonists and antagonists to the IGF-1R site are not fully clarified. However, the binding of ligands to the receptor site, preferably with an affinity in the order of 10^{-8}M or higher, is understood to arise from enhanced stereochemical complementarity relative to naturally occurring IGF-1 ligands.

Such stereochemical complementarity, pursuant to the present invention, is characteristic of a molecule that matches intra-site surface residues lining the groove of the receptor site as eneumerated by the coordinates set out in Figure 1. The residues lining the groove are depicted in Figure 2. By "match" we mean that the identified portions interact with the surface residues, for example, via hydrogen bonding or by enthalpy-reducing Van der Waals interactions which promote desolvation of the biologically active substance within the site, in such a way that retention of the biologically active substance within the groove is favoured energetically.

Substances which are complemetary to the shape of the receptor site characterised by amino acids positioned at atomic coordinates set out in

Figure 1 may be able to bind to the receptor site and, when the binding is sufficiently strong, substantially prohibit binding of the naturally occurring ligands to the site.

It will be appreciated that it is not necessary that the complementarity between ligands and the receptor site extend over all residues lining the groove in order to inhibit binding of the natural ligand. Accordingly, agonists or antagonists which bind to a portion of the residues lining the groove are encompassed by the present invention.

In general, the design of a molecule possessing stereochemical complementarity can be accomplished by means of techniques that optimize, either chemically or geometrically, the "fit" between a molecule and a target receptor. Known techniques of this sort are reviewed by Sheridan and Venkataraghavan, Acc. Chem Res. 1987 20 322; Goodford, J. Med. Chem. 1984 27 557; Beddell, Chem. Soc. Reviews 1985, 279; Hol, Angew. Chem. 1986 25 767 and Verlinde C.L.M.J & Hol, W.G.J. Structure 1994, 2, 577, the respective contents of which are hereby incorporated by reference. See also Blundell et al., Nature 1987 326 347 (drug development based on information regarding receptor structure).

Thus, there are two preferred approaches to designing a molecule, according to the present invention, that complements the shape of IGF-1R or a related receptor molecule. By the geometric approach, the number of internal degrees of freedom (and the corresponding local minima in the molecular conformation space) is reduced by considering only the geometric (hard-sphere) interactions of two rigid bodies, where one body (the active site) contains "pockets" or "grooves" that form binding sites for the second body (the complementing molecule, as ligand). The second preferred approach entails an assessment of the interaction of respective chemical groups ("probes") with the active site at sample positions within and around the site, resulting in an array of energy values from which three-dimensional contour surfaces at selected energy levels can be generated.

The geometric approach is illustrated by Kuntz et al., J. Mol. Biol. 1982 161 269, the contents of which are hereby incorporated by reference, whose algorithm for ligand design is implemented in a commercial software package distributed by the Regents of the University of California and further described in a document, provided by the distributor, which is entitled "Overview of the DOCK Package, Version 1.0,", the contents of which are

hereby incorporated by reference. Pursuant to the Kuntz algorithm, the shape of the cavity represented by the IGF-R1 site is defined as a series of overlapping spheres of different radii. One or more extant data bases of crystallographic data, such as the Cambridge Structural Database System maintained by Cambridge University (University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.) and the Protein Data Bank maintained by Brookhaven National Laboratory (Chemistry Dept. Upton, NY 11973, U.S.A.), is then searched for molecules which approximate the shape thus defined.

Molecules identified in this way, on the basis of geometric parameters, can then be modified to satisfy criteria associated with chemical complementarity, such as hydrogen bonding, ionic interactions and Van der Waals interactions.

The chemical-probe approach to ligand design is described, for example, by Goodford, J. Med. Chem. 1985 28 849, the contents of which are hereby incorporated by reference, and is implemented in several commercial software packages, such as GRID (product of Molecular Discovery Ltd., West Way House, Elms Parade, Oxford OX2 9LL, U.K.). Pursuant to this approach, the chemical prerequisites for a site-complementing molecule are identified at the outset, by probing the active site (as represented via the atomic coordinates shown in Fig. 1) with different chemical probes, e.g., water, a methyl group, an amine nitrogen, a carboxyl oxygen, and a hydroxyl. Favored sites for interaction between the active site and each probe are thus determined, and from the resulting three-dimensional pattern of such sites a putative complementary molecule can be generated.

The chemical-probe approach is especially useful in defining variants of a molecule known to bind the target receptor. Accordingly, crystallographic analysis of IGF-1 bound to the receptor site is expected to provide useful information regarding the interaction between the archetype ligand and the active site of interest.

Programs suitable for searching three-dimensional databases to identify molecules bearing a desired pharmacophore include: MACCS-3D and ISIS/3D (Molecular Design Ltd., San Leandro, CA), ChemDBS-3D (Chemical Design Ltd., Oxford, U.K.), and Sybyl/3DB Unity (Tripos Associates, St. Louis, MO).

Programs suitable for pharmacophore selection and design include: DISCO (Abbott Laboratories, Abbott Park, IL), Catalyst (Bio-CAD Corp., Mountain View, CA), and ChemDBS-3D (Chemical Design Ltd., Oxford, U.K.).

Databases of chemical structures are available from a number of sources including Cambridge Crystallographic Data Centre (Cambridge, U.K.) and Chemical Abstracts Service (Columbus, OH).

De novo design programs include Ludi (Biosym Technologies Inc., San Diego, CA), Sybyl (Tripos Associates) and Aladdin (Daylight Chemical Information Systems, Irvine, CA).

Those skilled in the art will recognize that the design of a mimetic may require slight structural alteration or adjustment of a chemical structure designed or identified using the methods of the invention.

The invention may be implemented in hardware or software, or a combination of both. However, preferably, the invention is implemented in computer programs executing on programmable computers each comprising a processor, a data storage system (including volatile and non-volatile memory and/or storage elements), at least one input device, and at least one output device. Program code is applied to input data to perform the functions described above and generate output information. The output information is applied to one or more output devices, in known fashion. The computer may be, for example, a personal computer, microcomputer, or workstation of conventional design.

Each program is preferably implemented in a high level procedural or object-oriented programming language to communicate with a computer system. However, the programs can be implemented in assembly or machine language, if desired. In any case, the language may be compiled or interpreted language.

Each such computer program is preferably stored on a storage medium or device (e.g., ROM or magnetic diskette) readable by a general or special purpose programmable computer, for configuring and operating the computer when the storage media or device is read by the computer to perform the procedures described herein. The inventive system may also be considered to be implemented as a computer-readable storage medium, configured with a computer program, where the storage medium so

configured causes a computer to operate in a specific and predefined manner to perform the functions described herein.

Compounds designed according to the methods of the present invention may be assessed by a number of *in vitro* and *in vivo* assays of hormone function. For example, the identification of IGF-1R antagonists of may be undertaken using a solid-phase receptor binding assay. Potential antagonists may be screened for their ability to inhibit the binding of europium-labelled IGF ligands to soluble, recombinant IGF-1R in a microplate-based format. Europium is a lanthanide fluorophore, the presence of which can be measured using time-resolved fluorometry. The sensitivity of this assay matches that achieved by radioisotopes, measurement is rapid and is performed in a microplate format to allow high-sample throughput, and the approach is gaining wide acceptance as the method of choice in the development of screens for receptor agonists/antagonists (see Apell et.al. J. Biomolec. Screening 3:19-27, 1998 : Inglese et. al. Biochemistry 37:2372-2377, 1998).

Binding affinity and inhibitor potency may be measured for candidate inhibitors using biosensor technology.

The IGF-1R antagonists may be tested for their ability to modulate receptor activity using a cell-based assay incorporating a stably transfected, IGF-1-responsive reporter gene [Souriau, C., Fort, P., Roux, P., Hartley, O., LeFranc, M-P. and Weill, M., 1997, Nucleic Acids Res. 25, 1585-1590]. An IGF-1-responsive, luciferase reporter gene has been assembled and transfected in 293 cells. The assay addresses the ability of IGF-1 to activate the reporter gene in the presence of novel ligands. It offers a rapid (results within 6-8 hours of hormone exposure), high-throughput (assay can be conducted in a 96-well format for automated counting) analysis using an extremely sensitive detection system (chemiluminescence). Once candidate compounds have been identified, their ability to antagonise signal transduction via the IGF-1R can be assessed using a number of routine *in vitro* cellular assays such as inhibition of IGF-1-mediated cell proliferation, induction of apoptosis in the presence of IGF-1 and the ablation of IGF-1-driven anchorage-independent cell growth in soft agar [D'Ambrosio, C., Ferber, A., Resnicoff, M. and Baserga, R., 1996, Cancer Res. 56, 4013-4020]. Such assays may be conducted on the P6 cell line, a cell line highly responsive to IGF as a result of the constitutive overexpression of the IGF-1R

(45-50,000 receptors/cell, [Pietrzkowski, Z., Sell, C., Lammers, R., Ullrich, A. and Baserga, R.,1992, Cell Growth.Diff. 3, 199-205]). Ultimately, the efficacy of any antagonist as a tumour therapeutic may be tested *in vivo* in animals bearing tumour isografts and xenografts as described [Resnicoff, M., Burgaud, J-L., Rotman, H. L., Abraham, D. and Baserga, R., 1995, Cancer Res. 55, 3739-3741; Resnicoff, M., Sell, C., Rubini, M., Coppola, D., Ambrose, D., Baserga, R. and Rubin, R., 1994 Cancer Res. 54: 2218-2222].

Tumour growth inhibition assays may be designed around a nude mouse xenograft model using a range of cell lines. The effects of the receptor antagonists and inhibitors may be tested on the growth of subcutaneous tumours.

A further use of the structure of the IGF-1R fragment described here is in facilitating structure determination of a related protein, such as a larger fragment of this receptor, another member of the insulin receptor family or a member of the EGF receptor family. This new structure may be either of the protein alone, or in complex with its ligand. For crystallographic analysis this is achieved using the method of molecular replacement (Brunger, Meth. Enzym. 1997 276 558-580, Navaza and Saludjian, *ibid.* 581-594, Tong and Rossmann, *ibid.* 594-611, Bentley, *ibid.* 611-619) in a program such as XPLOR. In this procedure diffraction data is collected from a crystalline protein of unknown structure. A transform of these data (Patterson function) is compared with a Patterson function calculated from a known structure. Firstly, the one Patterson function is rotated on the other to determine the correct orientation of the unknown molecule in the crystal. The translation function is then calculated to determine the location of the molecule with respect to the crystal axes. Once the molecule has been correctly positioned in the unit cell initial phases for the experimental data may be calculated. These phases are necessary for calculation of an electron density map from which structural differences may be observed and for refinement of the structure. Due to limitations in the method the search molecule must be structurally related to that which is to be determined. However it is sufficient for only part of the unknown structure (e.g. < 50%) to be similar to the search molecule. Thus the three dimensional structure of IGF-1R residues 1-462 may be used to solve structures consisting of related receptors, enabling a program of drug design as outlined above.

In summary, the general principles of receptor-based drug design can be applied by persons skilled in the art, using the crystallographic results presented above, to produce ligands of IGF-1R or other related receptors, having sufficient stereochemical complementarity to exhibit high affinity binding to the receptor site.

The present invention is further described below with reference to the following, non-limiting examples.

EXAMPLE 1

Expression, Purification and Crystallization of the IGF-1R Fragment.

Several factors hamper macromolecular crystallization including sample selection, purity, stability, solubility (McPherson, A., et al., 1995, Structure 3:759-768); Gilliland, G. L., & Ladner, J. E., 1996, Curr. Opin. Struct. Biol. 6:595-603), and the nature and extent of glycosylation (Davis, S. J., et al., 1993, Protein Eng. 6:229-232). Initial attempts to obtain structural data from soluble IGF-1R ectodomain (residues 1-906) protein, expressed in Lec8 cells (Stanley, P. 1989, Molec. Cellul. Biol. 9:377-383) and purified by affinity chromatography, produced large, well-formed crystals (1.0 mm x 0.2 mm x 0.2 mm) which gave no discernible X-ray diffraction pattern (unpublished data). Similar difficulties have been encountered with crystals of the structurally-related epidermal growth factor receptor (EGFR) ectodomain, which diffracted to only 6 Å, insufficient for the determination of an atomic resolution structure (Weber, W. et al., 1994, J Chromat 679:181-189). This prompted us to search for a fragment of IGF-1R that was more amenable to X-ray crystallographic studies.

The fragment expressed (residues 1-462) comprises the L1-cysteine-rich-L2 region of the ectodomain. The selected truncation position at Val462 is four residues downstream of the exon 6/exon 7 junction (Abbott, A. M., et al., 1992, J Biol Chem. 267:10759-10763), and occurs at a position where the sequences of the IR and the structurally related EGFR families diverge markedly (Lax, I., et al., 1988, Molec Cell Biol. 8:1970-1978; Ward, C. W., et al., 1995, Proteins: Struct., Funct., Genet. 22:141-153), suggesting that it represents a domain boundary. The expression strategy included use of the pEE14 vector (Bebbington, C. R. & Hentschel, C. C. G., 1987, In: Glover, D. M., ed. DNA Cloning. Academic Press, San Diego. Vol 3, p163) in glycosidase-defective Lec8 cells (Stanley, P., 1989, Molec. Cellul. Biol. 9:377-

383), which produce N-linked oligosaccharides lacking the terminal galactose and N-acetylneuraminic acid residues (Davis, S. J., et al., 1993, Protein Eng. 6:229-232; Liu, T., et al., 1996, J Biol Chem 271:33639-33646.). The construct contained a C-terminal c-myc affinity tag (Hoogenboom, H. R., et al., 1991, Nucl Acids Res. 19:4133-4137), which facilitated immunoaffinity purification by specific peptide elution and avoided aggressive purification conditions. These procedures yielded protein which readily crystallized after a further gel filtration purification step. This provided a general protocol to enhance crystallisation prospects for labile, multidomain glycoproteins.

The structure of this fragment is of considerable interest, since it contains the major determinants governing insulin and IGF-1 binding specificity (Gustafson, T. A. & Rutter, W. J., 1990, J. Biol. Chem. 265:18663-18667; Andersen, A. S., et al., 1990, Biochemistry, 29:7363-7366; Schumacher, R., et al., 1991, J. Biol. Chem. 266:19288-19295; Schumacher, R., et al., 1993, J. Biol. Chem. 268:1087-1094; Schäffer, L., et al., 1993, J. Biol. Chem. 268:3044-3047; Williams, P. F., et al., 1995, , J. Biol. Chem. 270:3012-3016), and is very similar to an IGF-1R fragment (residues 1-486) reported to act as a strong dominant negative for several growth functions and which induces apoptosis of tumour cells *in vivo* (D'Ambrosio, C., et al., 1996, Cancer Res. 56:4013-4020).

The expression plasmid pEE14/IGF-1R/462 was constructed by inserting the oligonucleotide cassette:

AatII

5' GACGTC GACGATGACGATAAG GAACAAAAACTCATC

D V D D D D K E Q K L I

(EK cleavage) (c-myc tail)

S E E D L N (Stop)

TCAGAAGAGGATCTGAAT TAGAATTC GACGTC 3'

EcoRI *AatII*

encoding an enterokinase cleavage site, c-myc epitope tag (Hoogenboom, H. R., et al., 1991, Nucleic acids Res. 19:4133-4137) and stop codon into the AatII site (within codon 462) of Igf-1r cDNA in the mammalian expression vector pECE (Ebina, Y., et al., 1985, Cell, 40:747-758; kindly supplied by W. J. Rutter, UCSF, USA), and introducing the DNA comprising the 5' 1521 bp of

the cDNA (Ullrich, A., et al., 1986, EMBO J. 5:2503-2512) ligated to the oligonucleotide cassette into the EcoRI site of the mammalian plasmid expression vector pEE14 (Bebbington, C. R. & Hentschel, C. C. G., 1987, In: Glover, D. M., ed. DNA Cloning. Academic Press, San Diego. Vol 3, p163; Celltech Ltd., UK). Plasmid pEE14/IGF-1R/462 was transfected into Lec8 mutant CHO cells (Stanley, P. 1989, Molec. Cellul. Biol. 9:377-383) obtained from the American Tissue Culture Collection (CRL:1737), using Lipofectin (Gibco-BRL). Cell lines were maintained after transfection in glutamine-free medium (Glascow modification of Eagle's medium (GMEM; ICN Biomedicals, Australia) and 10% dialysed FCS (Sigma, Australia) containing 25 μM methionine sulphoximine (MSX; Sigma, Australia) as described (Bebbington, C. R. & Hentschel, C. C. G., 1987, In: Glover, D. M., ed. DNA Cloning. Academic Press, San Diego. Vol 3, p163). Transfectants were screened for protein expression by Western blotting and sandwich enzyme-linked immunosorbent assay (ELISA) (Cosgrove, L., et al., 1995,) using monoclonal antibody (Mab) 9E10 (Evan et al., 1985) as the capture antibody, and either biotinylated anti-IGF-1R Mab 24-60 or 24-31 for detection(Soos et al., 1992; gifts from Ken Siddle, University of Cambridge, UK). Large-scale cultivation of selected clones expressing IGF-1R/462 was carried out in a Celligen Plus bioreactor (New Brunswick Scientific, USA) containing 70 g Fibra-Cel Disks (Sterilin, UK) as carriers in a 1.25 L working volume. Continuous perfusion culture using GMEM medium supplemented with non-essential amino acids, nucleosides, 25 μM MSX and 10% FCS was maintained for 1 to 2 weeks followed by the more enriched DMEM/F12 without glutamine, with the same supplemention for the next 4-5 weeks. The fermentation production run was carried out three times under similar conditions, and resulted in an estimated overall yield of 50 mg of receptor protein from 430 L of harvested medium. Cell growth was poor during the initial stages of the fermentation when GMEM medium was employed, but improved dramatically following the switch to the more enriched medium. Target protein productivity was essentially constant during the period from ~100 to 700 h of the 760 h fermentation, as measured by ELISA using Mab 9E10 as the capture antibody and biotinylated Mab 24-31 as the developing antibody.

Soluble IGF-1R/462 protein was recovered from harvested fermentation medium by affinity chromatography on columns prepared by coupling Mab 9E10 to divinyl sulphone-activated agarose beads (Mini Leak;

Kem En Tec, Denmark) as recommended by the manufacturer. Mini-Leak Low and Medium affinity columns with antibody loadings of 1.5-4.5 mg/ml of hydrated matrix were obtained, with the loading range of 2.5-3 mg/ml giving optimal performance (data not shown). Mab 9E10 was produced by growing hybridoma cells (American Tissue Culture Collection) in serum-free medium in the Celligen Plus bioreactor and recovering the secreted antibody (4 g) using protein A glass beads (Prosep-A, Bioprocessing Limited, USA). Harvested culture medium containing IGF-1R/462 protein was adjusted to pH 8.0 with Tris-HCl (Sigma), made 0.02% (w/v) in sodium azide and passed at 3-5 ml/min over 50 ml Mab 9E10 antibody columns at 4° C. Bound protein was recovered by recycling a solution of 2-10 mg of the undecamer c-myc peptide EQKLISEEDLN (Hoogenboom et al., 1991) in 20 ml of Tris-buffered saline containing 0.02% sodium azide (TBSA). Between 65% and 75% of the product was recovered from the medium as estimated by ELISA, with a further 15-25% being recovered by a second pass over the columns. Peptide recirculation (~10 times) through the column eluted bound protein more efficiently than a single, slower elution. Residual bound protein was eluted with sodium citrate buffer at pH 3.0 into 1 M Tris HCl pH 8.0 to neutralize the eluant, and columns were re-equilibrated with TBSA.

Gel filtration over Superdex S200 (Pharmacia, Sweden), of affinity-purified material showed a dominant protein peak at ~63 kDa, together with a smaller quantity of aggregated protein (Figure 3a). The peak protein migrated primarily as two closely spaced bands on reduced , sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE; Figure 3b), reacted positively in the ELISA with both Mab 24-60 and Mab 24-31, and gave a single sequence corresponding to the N-terminal 14 residues of IGF-1R. No binding of IGF-1 or IGF-2 could be detected in the solid plate binding assay (Cosgrove et al., 1995, Protein Express Purif. 6:789-798). The IGF-1R/462 fragment was further purified by ion-exchange chromatography on Resource Q (Pharmacia, Sweden). Using shallow salt gradients, protein enriched in the slowest migrating SDS-PAGE band was obtained (data not shown), which formed relatively large, well-formed crystals (see below). Isoelectric focussing showed the presence of one major and two minor isoforms. Protein purified on Resource Q with an isocratic elution step of 0.14 M NaCl in 20 mM TrisCl at pH 8.0 (fraction 2, Figure 4) showed less heterogeneity on isoelectric focussing (Figure 4 inset) and SDS-PAGE (data not shown), and

produced crystals of sufficient quality for structure determination (see below).

Crystals were grown by the hanging drop vapour diffusion method using purified protein concentrated in Centricon 10 concentrators (Amicon Inc, USA) to 5-10 mg/ml in 10-20 mM Tris-HCl pH 8.0 and 0.02% (w/v) sodium azide, or 100 mM ammonium sulfate and 0.02% (w/v) sodium azide. Crystallization conditions were initially identified using the factorial screen (Jancarik, J. & Kim, S.-H.,1991, J Appl Cryst 24:409-411),and then optimised. Crystals were examined on an M18XHF rotating anode generator (Siemens, Germany) equipped with Franks mirrors (MSC, USA) and RAXIS IIC and IV image plate detectors (Rigaku, Japan).

From the initial crystallization screen of this protein, crystals of about 0.1 mm in size grew in one week. Upon refining conditions, crystals of up to 0.6 x 0.4 x 0.4 mm could be grown from a solution of 1.7-2.0 M ammonium sulfate, 0.1 M HEPES pH 7.5. The crystals varied considerably in shape and diffraction quality, growing predominantly as rhombic prisms with a length to width ratio of up to 5:1, but sometimes as rhombic bipyramids, the latter form being favoured when using material which had been eluted from the Mab 9E10 column at pH 3.0. Each crystal showed a minor imperfection in the form of very faint lines from the centre to the vertices. Protein from dissolved crystals did not appear to be different from the protein stock solution when run on an isoelectric focusing gel. Upon X-ray examination, the crystals diffracted to 3.0-4.0 Å and were found to belong to the space group $P2_12_12_1$ with a = 76.8 Å, b = 99.0 Å, c = 119.6 Å. In the diffraction pattern, the crystal variability noted above was manifest as a large (1-2°) and anisotropic mosaic spread, with concomitant variation in resolution. To improve the quality of the crystals, they were grown in the presence of various additives or were recrystallized. These methods failed to substantially improve the crystal quality although bigger crystals were obtained by recrystallization. The variability in crystal quality appeared to be due to protein heterogeneity, as demonstrated by the observation that more highly purified protein, eluted isocratically from the Resource Q column and showing one major band on isoelectric focusing (Figure 4 inset), produced crystals of sufficient quality for structure determination. These crystals diffracted to 2.6 Å resolution with cell dimensions, a = 77.0 Å, b = 99.5 Å, c = 120.1 Å and mosaic spread of 0.5°. Heavy metal derivatives of the IGF-

1R/462 crystals have been obtained and are leading to the determination of an atomic resolution structure of this fragment, which contains the L1, cysteine-rich and L2 domains of human IGF-1R.

EXAMPLE 2

Structure of the IGF-1R/1-462

Crystals were cryo-cooled to-170°C in a mother liquor containing 20% glycerol, 2.2 M ammonium sulfate and 100 mM Tris at pH 8.0. Native and derivative diffraction data were recorded on Rigaku RAXIS IIc or IV area detectors using copper Kα radiation from a Siemens rotating anode generator with Yale/MSC mirroroptics. The space group was $P2_12_12_1$ with a = 77.39 Å, b = 99.72 Å, and c = 120.29 Å. Data were reduced using DENZO and SCALEPACK (Otwinowski, Z. & Minor, W., 1996, Mode.Meth. Enzym. 276:307-326). Diffraction was notably anisotropic for all crystals examined.

Phasing by multiple isomorphous replacement(MIR) was performed with PROTEIN (Steigeman, W. Dissertation (Technical Univ. Munich, 1974) using anomalous scattering for both UO2 and PIP derivatives. Statistics for data collection and phasing are given in Table 1. In the initial MIR map regions of protein and solvent could clearly be seen, but the path of the polypeptide was by no means obvious. That map was subject to solvent flattening and histogram matching in DM (Cowtan, K.,1994, Joint CCP4 and ESF-EACBM newslett. Protein Crystallogr. 31:34-38). The structure was traced and rebuilt using O (Jones, T. A., et al., 1991, Acta Crystallogr. A47:110-119) and refined with X-PLOR 3.851 (Brunger, A. T., 1996, X-PLOR ReferenceManual 3.851, Yale Univ., New Haven, CT). After 5 rounds of rebuilding and energy minimisation the R-factor dropped to 0.279 and Rfree = 0.359 for data 7-2.6 Å resolution. The current model contains 458 amino acids and 3 N-linked carbohydrates but no solvent molecules. For residues with B(Ca) > 70, Å atomic positions are less reliable (37-42, 155-159, 305, 336-341, 404-406,453-458). There is weak electron density for residues 459-461, but the c-myc tail appears completely disordered.

The 1-462 fragment consists of the N-terminal three domains of IGF-1R (L1, cys-rich, L2), and contains regions of the molecule which dictate ligand specificity (17-23). The molecule adopts a reasonably extended structure (approximately 40 x 48 x 105 Å) with domain 2 (cys-rich region)

making contact along the length of domain 1 (L1) but very little contact with the third domain (L2) (see Figure 5). This leaves a space at the centre of the molecule of approximately 24 Å x 24 Å x 24 Å which is bounded on three sides by the three domains of the molecule. The space is of sufficient size to accommodate the ligand, IGF-1.

Table 1 Summary of Crystallographic data

Data set[a]	Resol. (Å)	Mean I/s	R_{merge}[b]	Completeness (multiplicity)	No. of sites	R_{cullis}[c]	Phasing power[d]	FOMe
Native	2.6	18.7	0.064	0.996 (4.1)				0.47 / 0.71
PIP	3.0	15.8	0.060	0.982 (2.2)	3	0.66	1.71	
UO2Ac2	4.5	7.5	0.095	0.989 (2.3)	2	0.82	1.17	

Refinement resolution (Å)	No of refl. (free)	No. of Atoms	R_{cryst}[f]	R_{free}[f]	Bonds[g] (Å)	Angles[g] (Å)
7.0-2.6	24270 (2693)	3903	0.237	0.304	0.017	0.048

[a] PIP, Di-μ-iodobis(ethylenediamine)diplatinum dinitrate; UO_2Ac_2, Uranyl acetate.

[b] $R_{merge} = \Sigma_{\mathbf{h}}\Sigma_j |I_{\mathbf{h},j}-I_{\mathbf{h}}| / \Sigma_{\mathbf{h}}\Sigma_j I_{\mathbf{h}}$, where $I_{\mathbf{h},j}$ is an intensity measurement j and $I_{\mathbf{h}}$ is the mean intensity for that reflection **h**.

[c] $R_{cullis} = \Sigma_{\mathbf{h}} ||F_{PH}-F_P| - |F_{Hcalc}||/\Sigma_{\mathbf{h}}||F_{PH}|-|F_P||$, where F_{PH}, F_P and F_{Hcalc} are, respectively, derivative, native and heavy atom structure factors for centric reflections **h**.

[d] Phasing power = $\Sigma_{\mathbf{h}} |F_{Hcalc}|/\Sigma_{\mathbf{h}}\varepsilon$, where F_{Hcalc} is defined above and ε is the lack of closure.

[e] FOM(figure of merit) = $\langle\cos(\Delta\alpha_{\mathbf{h}})\rangle$, where $\Delta\alpha_{\mathbf{h}}$ is the error in the phase angle for reflection **h**. Values are given before and after density modification at 3.0 and 2.8 Å resolution, respectively.

[f] R_{cryst} and R_{free} are defined in Brunger, A.T. *XPLOR* reference manual 3.851 (Yale Univ., New Haven, CT, 1996)

g r.m.s. deviation from ideal bond and angle-related (1-3) distances.

The L domains

Each of the L domains (residues 1-150 and300-460) adopts a compact shape (24 x 32 x 37 Å) consisting of a single-stranded right handed β-helix and capped on the ends by short α-helices and disulfide bonds. The body of the domain looks like a loaf of bread, with the base formed from a flat six-stranded β-sheet, 5 residues long and the sides being β-sheets three residues long (Figures 5 & 6). The top is irregular, but in places is similar for the two domains. The two domains are superposable with an rms deviation in Cα positions of 1.6 Å for 109 atoms (Figure 7). Although this fold is reminiscent of other β-helix proteins it is much simpler and smaller with very few elaborations, and thus it represents a new superfamily of domains. One notable difference between the two domains is that the indole ring of Trp 176 from the cys-rich region (Figure 6b) is inserted into the hydrophobic core of L1, and the C-terminal helix is only vestigial (Figure 8). For the insulin receptor family the sequence motif of residues which form the Trp pocket in L1 does not occur in L2 (Figure 6a). However in the EGF receptor, which has an additional cys-rich region after the L2 domain (14, 15), the pocket motif can be found in both L domains and the Trp is conserved in both cys-rich regions (Figure 6b).

The repetitive nature of the β-helix is reflected in the sequence and the first five turns were correctly identified by Bajaj, M., et al. (1987, Biochim.Biophys. Acta 916:220-226), the conserved Gly residues being found in turns making one bottom edge of the domain. However, their conclusions about the fold were incorrect. The"helix-like" repeat is actually a pair of bends at the top edge of the domain. In their Motif V, the Gly is not in a bend but is followed by the insertion of a conserved loop of 7-8 residues (see Figure 6a). Glycine is structurally important in the Gly bends as mutation of these residues compromises folding of the receptor [van der Vorm, E.R., et al., 1992, J. Biol. Chem. 267, 66-71; Wertheimer, E. et al., 1994, J. Biol. Chem. 269, 7587-7592].

Comparison of the L domains with other right-handed β-helix structures such as pectate lyase (Yoder, M. D., et al., 1993,.Structure, 1:241-251-1507) and the p22 tailspike protein (Steinbacher, S., et al., 1997, J.Mol. Biol. 267:865-880) shows some striking similarities as well as differences. In

all cases the ends of the domain are capped by α-helices, but the L domains also have a disulphide bond at each end to hold the termini. The other β-helix domains are considerably longer and have significant twist to their sheets, while the L domains have flat sheets. Although the sizes of the helix repeats are similar (here 24-25 residues vs 22-23 for pectate lyase) the cross-sections are quite different. The L domains have a rectangular cross-section, while pectate lyase and p22 tailspike protein are V-shaped, and have many, and sometimes quite large, insertions (Yoder, M. D., et al., 1993, Structure, 1:241-251-1507; Steinbacher, S., et al., 1997, J.Mol. Biol. 267:865-880). In the hydrophobic core a common feature is the stacking of aliphatic residues from successive turns of the β-helix, and near the C-terminus of each L domain there is also a short Asn ladder, reminiscent of the long Asn ladder observed in pectate lyase (Yoder, M. D., et al., 1993, Structure 1:241-251-1507). On the opposite side of the L domains the Gly bend, as well as the two bends and sheet preceding it, have no counterpart in the other β-helix domains. Thus although the L domains are built on similar principles to the other β-helix domains they constitute a separate superfamily.

The cys-rich domain

The cys-rich domain is composed of eight disulfide-bonded modules (Figure 6b), the first of which sits at the end of L1, while the remainder make a curved rod running diagonally across L1 and reaching to L2 (Figure 5). The strands in modules 2-7 run roughly perpendicular to the axis of the rod in a manner more akin to laminin (Stetefeld, J., et al.,1996, J.Mol.Biol. 257:644-657) than to TNF receptor (Banner, D. W., et al., 1993, Cell, 73:431-445), but the modular arrangement of the cys-rich domain is different to those of other cys-rich proteins for which structures are known. The first 3 modules of IGF-1R have a common core, containing a pair of disulfide bonds, but show considerable variation in the loops (Figure 6b). The connectivity of these modules is the same as in the first half of EGF (Cys 1-3and 2-4), but their structures do not appear to be closely related to any member of the EGF family. Modules 4 to 7 have a different motif, a β-finger, and best match residues 2152-2168 of fibrillin (Dowling, A. K., et al., 1996, Cell, 85:597-605). Each is composed of three polypeptide strands, the first and third being disulfide bonded and the latter two forming a β-ribbon. The β-ribbon of each β- finger module lines up antiparallel to form a tightly twisted 8-stranded β-sheet (Figures 5 and 8). Module 6 deviates from the common pattern,with

the first segment being replaced by an α-helix followed by a large loop that is likely to have a role in ligand binding (see below). As module 5 is most similar to module 7 it is possible that the four modules arose from serial gene duplications. The final module is a disulfide-linked bend of five residues.

The fact that the two major types of cys-rich modules occur separately implies that these are the minimal building blocks of cys-rich domains found in many proteins. Although it can be as short as 16 residues, the motif of modules 4-7 is clearly distinct, and capable of forming a regular extended structure. Thus cys-rich domains such as these can be considered as being made of repeat units each composed of a small number of modules.

Hormone binding

Attempts have been made to locate the IGF-1 (and insulin) binding site by examining natural (Taylor, S. I., 1992, Diabetes, 41:1473-1490) and site-directed mutants (Williams, P. F., et al., 1995, J. Biol. Chem. 270:3012-3016; Mynarcik, D. C et al., 1996, J. Biol. Chem. 271:2439-2442; Mynarcik, D. C., et al., 1997, J. Biol. Chem. 272:2077-2081), chimeric receptors (Andersen, A. S., et al., 1990, Biochemistry 29:7363-7366; Gustafson, T. A., & Rutter, W. J., 1990, J. Biol. Chem. 265:18663-18667; Schäffer, L., et al.,1993, J. Biol. Chem. 268:3044-3047; Schumacher, R., 1993, J. Biol. Chem. 268:1087-1094; Kjeldsen, T., et al., 1991, Proc. Natl Acad. Sci. USA, 88:4404-4408) and by crosslinking studies (Wedekind, F., et al., 1989, Biol. Chem Hoppe-Seyler, 370:251-258; Fabry, M., 1992, J. Biol. Chem. 267:8950-8956; Waugh, S. M., et al., 1989, Biochemistry, 28:3448-3458; Kurose, T., et al., 1994),.J. Biol. Chem.269:29190-29197-34). IGF-1R/IR chimeras not only show which regions of the receptors account for ligand specificity, but also provide an efficient means of identifying some parts of the hormone binding site. Paradoxically, regions controlling specificity are not the same for insulin and IGF-1. Replacing the first 68 residues of IGF-1R with those of IR confers insulin-binding ability on the chimeric IGF-1R (Kjeldsen, T., et al., 1991, Proc. Natl Acad. Sci. USA, 88:4404-4408), and replacing residues 198-300 in the cys-rich region of IR with the corresponding residues 191-290 of IGF-1R allows the chimeric receptor to bind IGF-1 (Schäffer, L., et al.,1993, J. Biol. Chem. 268:3044-3047). Thus a receptor can be constructed which binds both IGF-1 and insulin with near native affinity. From the structure it is clear that if the hormone bound in the central space it could contact both these regions.

From analysis of a series of chimeras examined by Gustafson, T. A., & Rutter, W. J. (J. Biol. Chem. 265:18663-18667, 1990), the specificity determinant in the cys-rich region can be limited further to residues 223-274. This region corresponds to modules 4-6, and includes a large and somewhat mobile loop (residues 255-263, mean B[Cα atoms] = 57 Å2) which extends into the central space (see Figure 5). In IR this loop is four residues bigger, and is stabilised by an additional disulfide bond (Schäffer, L. & Hansen, P.H.,1996, Exp. Clin. Endocrinol. Diabetes, 104: Suppl. 2, 89). The larger loop of IR may serve to exclude IGF-1 from the hormone binding site while allowing the smaller insulin molecule to bind. It is interesting to note that mosquito IR homologue, which has a loop two residues larger than the mammalian IRs, also appears to bind insulin but not IGF-1 (Graf, R., et al., 1997, Insect Molec.Biol. 6:151-163). Analysis of the structure indicates that the insulin/IGF-1 specificity is controlled by residues in this loop (amino acids 253-272 in IGF-1R; amino acids 260-283 in IR)

As chimeras only address residues which differ between the two receptors, a more precise analysis of the site can be obtained from single site mutants. In particular, from an alanine-replacement study, four regions of L1 important for insulin binding were identified (Williams, P. F., et al., 1995, J. Biol. Chem. 270:3012-3016). The first three are at similar positions on successive turns of the β-helix and the fourth lies on the conserved bulge on the large β-sheet. Thus there is a footprint for insulin binding to the L1 domain which lies on the first half of the large β-sheet facing into the central space. Residues further along the sheet which are conserved in IGF-1R could also be important. The conservative substitution of leucine for methionine at residue 119 of IR (113 of IGF-1R) causes a mild form of leprechaunism [Hone, J. et al., 1994, J. Med. Genet. 31, 715-716]. This residue is buried, and the mutation could perturb neighbouring residues to affect insulin binding.

The axis of the L2 domain is perpendicular to that of the L1 domain, and the N-terminal end of its β-helix is presented to the hormone-binding site. On this face of the L2 domain the only mutation studied so far is the naturally occurring IR mutant, S323L, which gives rise to Rabson-Mendehall syndrome and severe insulin resistance (Roach, P.,1994, Diabetes 43:1096-1102). As this mutant only affects insulin binding and not cell-surface expression, residue 323 of IR (residue 313 of IGF-1R) is probably at or near the binding site. Structurally this residue lies in the middle of a region

(residues 309-318 of IGF-1R) which is conserved in both IR and IGF-1R, and the surrounding region, 332-345 (of IGF-1R), is also quite well conserved in the these receptors (Figure 6a). Therefore this region is quite likely to form part of the hormone-binding site, but would not have been detected by chimeras. It is interesting to note that in this region IRR is not as well conserved as the other two receptors (Shier, P. & Watt, V.M., 1989, J.Biol.Chem. 264:4605-14608).

The distance from this putative hormone-binding region on L2 to that found on L1 is about 30 Å (Figure 5). Thus L1 and L2 appear too far apart to bind IGF-1 or insulin. However, in the crystal structure there is a deep cleft between part of the cys-rich domain (residue 262)and L2 (residue 305), and this cleft is occupied by a loop from a neighbouring molecule. Thus it seems probable that the position of the L2 domain in the receptor structure or the hormone-receptor complex adopts a different position with respect to the cys-rich domain than that found in the crystal. The movement required to bring L2 sufficiently close to L1 is small, namely a rotation of approximately 25° about residue 298.

A number of IR mutants have been identified which constitutively activate the receptor, and the majority of these are found in the α chain. Curiously all α chain mutants involve changes to or from proline or the deletion of an amino acid, implying that they cause local structural rearrangements. The mutation R86N is similar to wild type, but R86P reduces cell-surface expression and insulin binding while constitutively activating autophosphorylation [Grønskov, K. et al., 1993, Biochem. Biophys. Res. Commun. 192, 905-911]. The proline mutation probably disturbs residues preceding 87 which lie in the interface between the L1 and cys-rich domains, but it could also affect insulin binding. In the cys-rich domain residues 233, 281, 244 and 247 of IR are not conserved in IGF-1R (Figure 6b), yet L233P [Klinkhamer, M.P. et al., 1989, EMBO J. 8, 2503-2507], deletion of N281 [Debois-Mouthon, C. et al., 1996, J. Clin. Endochronol. Metab. 81, 719-727] or the triple mutant P243R, P244R and H247D [Rafaeloff, R. et al., 1989, J. Biol. Chem. 264, 15900-15904] cause constitutive kinase activation. Due to their locations each of these three mutants appears likely to compromise the folding of a β-finger domain and, in turn, the structural integrity of the rod-like cys-rich domain. The structural ramifications of these mutations could be significant for the whole receptor ectodomain, as disturbing the L1/cys-

rich interface or distorting the rod-like domain could affect the relative position of L1 and the cys-rich domain in this context.

L1 has been further implicated, as deletion of K121 on the opposite side of L1 from the cys-rich domain was also found to cause autophosphorylation [Jospe, N. et al., 1994, J. Clin. Endochronol. Metab. 79, 1294-1302]. By contrast this mutation does not affect insulin binding. Thus a possible mechanism emerges for insulin binding and signal transduction. When insulin binds between L1 and L2 it modifies the relative position of L1 and the cys-rich domain in the receptor, perhaps by hinge motion between L2 and the cys-rich domain like that suggested above, and the structural rearrangement is transmitted across the plasma membrane. In the absence of insulin the same signal can be initiated by mutations in the cys-rich region or at the L1/cys-rich interface, but at the expense on insulin binding. The signal can also be initiated more directly by mutations on the opposite side of L1 which affect the interaction of L1 with other parts of the ectodomain, possibly the other half of the receptor dimer.

Ligand Studies

Although there is no structural information about an IGF-1/IGF-1R complex a number of studies have probed the nature of this interaction. Results from cross-linking experiments with IGF-1 and insulin and their cognate receptors are consistent with the hormone binding site proposed above. For example B29 of insulin can be cross-linked to the cys-rich region (residues 205-316((Yip, C. C., et al., 1988, Biochim. Biophys. Res. Commun. 157:321-329) or the L1 domain (Wedekind, F., et al., 1989, Biol. Chem Hoppe-Seyler, 370:251-258). However, these two regions are reasonably well separated, and those studies may indicate that B29 is mobile. Other studies unfortunately do not map the site any more precisely.

Analogues and site-directed mutants of IGF-1 and IGF-2 have been more fruitful. IGF-1 and IGF-2 contain two extra regions relative to insulin, the C region between B and A and a D peptide at the C-terminus. For IGF-1, replacement of the C region by a four Gly linker reduced affinity for IGF-1R by a factor of 40 but increased affinity for IR 5-fold (Bayne, M.L.,et al., 1988, J. Biol.Chem. 264:11004-11008). Changes in affinity are consistent with the deletion in IGF-1 complementing differences in the cys-rich regions of IGF-1R and IR noted above. Mutation of residues either side of the C region (residue 24 for IGF-1 [Cascieri, M.A., et al., 1988, Biochemistry 27:3229-

3233], residues 27,43 for IGF-2, [Sakano, K., et al., 1991, J. Biol. Chem. 266:20626-20635]) also has deleterious effects on the affinity of the hormone for IGF-1R, as has truncation of the nearby D peptide in IGF-2 (Roth, B.V., et al., 1991, Biochem. Biophys. Res. Commun. 181:907-914).

Insulin has been extensively mutated. Binding studies [summarised in Kristensen, C. et al., 1997, J. Biol. Chem. 272, 12978-12983] indicate that insulin may bind its receptor via a hydrophobic patch (residues A2, A3, A19, B8, B11, B12, B15 and possibly B23 & B24). However this patch is normally buried, and requires the removal of the B chain's C-terminus from the observed position. Assuming IGF-1, IGF-2 and insulin bind their receptors in the same orientation, these data suggest an approximate orientation for the hormone when bound to the receptor.

One notable feature of IGF-1 and IGF-2 is the large number of charged residues and their uneven distribution over the surface. Basic residues are predominantly found in the C region and, in solution, this region is not well ordered in either IGF-1 or -2 (Sato, A., et al., 1993, Int J Peptide Protein Res. 41:433-440; Torres, A. M., et al., 1995,J. Mol. Biol. 248:385-401). In contrast the binding site of the receptor has a sizable patch of acidic residues in the corner where the cys-rich domain departs from L1. Other acidic residues which are specific to this receptor are found along the inside face of the cys-rich domain and the loop (residues 255-263) extending from module 6. Thus it is possible that electrostatic interactions play an important part in IGF-1 binding, with the C region binding to the acidic patch of the cys-rich region near L1 and the acidic patch on the other side of the hormone directed towards a small patch of basic residues (residues 307-310) on the N-terminal end of L2.

Although the structure of this fragment gives significant information about the nature of the hormone binding site, residues outside this region have also been shown to affect binding of ligand. A number of studies have implicated residues 704-715 of IR (Mynarcik, D. C et al., 1996, J. Biol. Chem. 271, 2439-2442; Kurose, T., et al., 1994, J. Biol. Chem.269:29190-29197). These residues could contact insulin on one of the sides left open in the current structure. Using insulin labelled at the B1 residue, Fabry, M., et al.,(1992, J. Biol. Chem. 267:8950-8956) cross-linked insulin to the fragment 390-488, part of which is not near the site as described. The explanation for this could be either the region 390-488 reaches back to the hormone binding

site, or this region could contact another hormone bound to the other half of the receptor. Further structural information is needed to establish how these other regions contact the hormone and to elucidate how binding of the hormone is communicated to the kinase inside the cell.

The structure of the L1-cys-rich-L2 domains of IGF-1R presented here represents the first structural information for the extracellular portion of a member of the insulin receptor family. The L domains display a novel fold which is common to the EGF receptor family, and the modular architecture of the cys-rich domain implies that smaller building blocks should be used to describe the composition of cysteine-rich domains. This fragment contains the major specificity determinants of receptors of this class for their ligands. It has an elongated structure with a space in the middle which could accommodate the ligand. The three sides of this site correspond to regions which have been implicated in hormone binding. Although other sites are present in the receptor ectodomain which interact with the ligand, this structure gives us an initial view of how the insulin, IGF-1 and IGF-2 might interact with their cell surface receptors to control their metabolic and mitogenic effects

Such information will provide valuable insight into the structure of the corresponding domains of the IR and insulin receptor-related receptor as well as members of the related EGFR family (Bajaj, M., et al., 1987, Biochim Biophys Acta 916:220-226; Ward, C. W. et al., 1995, Proteins: Struct Funct Genet 22:141-153).

EXAMPLE 3

Prediction of 3D Structure of the Corresponding Domains of IRR and IR Based on Structure of IGF-1R Fragment.

The sequence identities between the different members of the insulin receptor family are sufficient to allow accurate sequence alignments to facilitate 3D structure predictions by homology modelling. The alignments of the ectodomains of human IGF-1R, IR, and IRR are shown in Figure 9.

EXAMPLE 4

Single-Molecule Imaging of Human Insulin Receptor Ectodomain and its Fab Complexes

Cloning and expression of hIR -11 ectodomain protein

A full length clone of the human IR exon -11 form (hIR -11) was prepared by exchanging an Aat II fragment, nucleotides 1195 to 2987 , of the

exon +11 clone (plasmid pET; Ellis et al., 1986; gift from Dr W. J. Rutter, UCSF) of hIR (Ebina et al., 1985, *Cell* **40,** 747-758) with the equivalent Aat II fragment from a plasmid (pHIR/P12-1, ATCC 57493) encoding part of the extracellular domain and the entire cytoplasmic domain of hIR -11 (Ullrich et al., 1985, *Nature* **313** , 756-761). The ectodomain fragment of hIR -11 (2901 bp, coding for the 27 residue signal sequence and residues His1-Asn914) was produced by SalI and SspI digestion and inserted into the mammalian expression vector pEE6.HCMV-GS (Celltech Limited, Slough, Berkshire, UK) into which a stop codon linker had been inserted, as described previously (Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798) for the hIR exon +11 ectodomain.

The resulting recombinant plasmid pHIR II (2 μg) was transfected into glycosylation-deficient Chinese hamster ovary (Lec 8) cells (Stanley, 1989, *Molec. Cellul. Biol.* **9,** 377-383) with Lipofectin (Gibco-BRL). After transfection, the cells were maintained in glutamine-free medium GMEM (ICN Biomedicals, Australia) as described previously (Bebbington & Hentschel, 1987, In *DNA Cloning* (Glover, D., ectodomain.), Vol III, Academic Press, san Diego; Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798). Expressing cell lines were selected for growth in GMEM with 25 μM methionine sulphoximine (MSX, Sigma). Transfectants were screened for protein expression using sandwich ELISA with anti-IR monoclonal antibodies 83-7 and 83-14. Metabolic labelling of cells, immunoprecipitations, insulin binding assays and Scatchard analyses were performed as described previously for the exon +11 form of hIR ectodomain (Cosgrove et al., 1995, , *Protein Expression and Purification* **6,** 789-798).

hIR -11 ectodomain production and purification

The selected clone (inoculum of 1.28 x 108 cells) was grown in a spinner flask packed with 10 g of Fibra-cel disc carriers (Sterilin, U.K.) in 500 ml of GMEM medium containing 10% fetal calf serum (FCS) and 25 μM MSX. Selection pressure was maintained for the duration of the culture.

Ectodomain was recovered from harvested medium by affinity chromatography on immobilized insulin, and further purified by gel filtration chromatography on Superdex S200 (Pharmacia; 1 x 40 cm) in Tris-buffered saline containing 0.02% sodium azide (TBSA) as described previously (Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798). Solutions of purified hIR -11 ectodomain were stored at 4° C prior to use.

Production of Fab fragments and their complexes with ectodomain

Purification of Mabs 83-7, 83-14 and 18-44 from ascites fluid by affinity chromatography using Protein A-Sepharose, and the production of Fabs, were based on the methodologies described in Coligan et al.,1993, Current Protocols in Immunology, Vol 1, pp 2.7.1-2.8.9, Greene Publishing Associates & Wiley - Interscience, John Wiley and Sons. Fab was produced from monoclonal antibody by mercuripapain digestion for 1-4 h, followed by gel filtration on Superdex S200. Products were monitored by reducing and non-reducing SDS-PAGE. For 83-7 Mab, an IgG Type 1 monoclonal antibody, the bivalent (Fab)2' isolated by this method was reduced to monovalent Fab 83-7 by mild reduction with mM L-cysteine.HCl in 100 mM Tris pH 8.0 (Coligan et al., 1993, Current Protocols in Immunology, Vol 1, pp 2.7.1-2.8.9, Greene Publishing Associates & Wiley - Interscience, John Wiley and Sons).

Complexes of Fab with hIR -11 ectodomain were produced by mixing ~ 2.5 to 3.5 molar excess of Fab with hIR -11 ectodomain at ambient temperature in TBSA at pH 8.0. After 1-3 h, the complex was separated from unbound Fab by gel filtration over a Superdex S200 column in the same buffer.

Electron microscopy

Uncomplexed hIR -11 ectodomain and the Fab complexes described above were diluted in phosphate-buffered saline (PBS) to concentrations of the order of 0.01-0.03 mg/ml. Prior to dilution, 10% glutaraldehyde (Fluka) was added to the PBS to achieve a final concentration of 1% glutaraldehyde. Droplets of ~ 3ml of this solution were applied to thin carbon film on 700-mesh gold grids after glow-discharging in nitrogen for 30 s. After 1 min. the excess protein solution was drawn off and followed by application and withdrawal of 4-5 droplets of negative stain [2% uranyl acetate (Agar), 2% uranyl formate (K and K), 2% potassium phosphotungstate (Probing and Structure) adjusted to pH 6.0 with KOH, or 2% methylamine tungstate (Agar) adjusted to pH 6.8 with NH4OH]. In the case of both uranyl acetate and uranyl formate staining, an intermediate wash with 2 or 3 droplets of PBS was included prior to application of the stain. The grids were air-dried and

then examined at 60kV accelerating voltage in a JEOL 100B transmission electron microscope at a magnification of 100,000x. It was found that there was a typical thickness of negative stain in which Fabs were most easily seen. Hence areas for photography had to be chosen from particular zones of the grid. Electron micrographs were recorded on Kodak SO-163 film and developed in undiluted Kodak D19 developer. The electron-optical magnification was calibrated under identical imaging conditions by recording single-molecule images of the antigen-antibody complex of influenza virus neuraminidase heads and NC10 MFab (Tulloch et al., 1986, *J.Mol. Biol.* **190**, 215-225; Malby et al., 1994, *Structure*, **2**, 733-746).

Image processing

Electron micrographs showing particles in a limited number of identifiable projections were chosen for digitisation. Micrographs were digitised on a Perkin-Elmer model 1010 GMS PDS flatbed scanning microdensitometer with a scanning aperture (square) size of 20 mm and stepping increment of 20 mm corresponding to a distance of 0.2 nm on the specimen. Particles were selected from the digitised micrograph using the interactive windowing facility of the SPIDER image processing system (Frank et al., 1996, *J. Struct. Biol.* **116,** 190-199). Particles were scaled to an optical density range of 0.0 - 2.0 and aligned by the PSPC reference-free alignment algorithm (Marco et al., 1996, *Ultramicroscopy*, **66**, 5-10). Averages were then calculated over a subset of correctly aligned particles chosen interactively as being representative of a single view of the particle. The final average image presented here is derived from a library of 94 images.

Biochemical characterization of expressed hIR -11 ectodomain

The recombinant protein examined corresponded to the the first 914 residues of the 917 residue ectodomain of the exon -11 form of the human insulin receptor (Ullrich et al., 1986, *Nature* **313** , 756-761). Expressed protein was shown, by SDS-PAGE and autoradiography of immunoprecipitated product from metabolically labelled cells, to exist as a homodimeric complex of ~270 - 320 kDa apparent mass, which dissociated under reducing conditions into monomeric α and β' subunits of respective apparent mass ~120 kDa and ~35 kDa (data not shown).

Purified hIR -11 ectodomain, expressed in Lec8 cells and purified by affinity chromatography on an insulin affinity column, eluted as a symmetrical peak on a Superdex S200 gel filtration column (Figure 10). The

protein eluted with an apparent mass of ~400 kDa, calculated from a standard curve generated by the elution positions of standard proteins (not shown). As expected for protein expressed in Lec 8 cells, whose glycosylation defect produces truncated oligosaccharides (Stanley, 1989, . *Molec. Cellul. Biol.* **9,** 377-383), this value is less than the apparent mass (450 - 500 kDa) reported for hIR +11 ectodomain expressed in wild-type CHO-K1 cells (Johnson et al., 1988, *Proc. Natl Acad. Sci USA* **85,** 7516-7520; Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798).

Radioassay of insulin binding to purified ectodomain gave linear Scatchard plots and Kd values of 1.5 - 1.8 x 10-9 M, similar to the values of 2.4 - 5.0 x 10-9 M reported for the hIR -11 ectodomain (Andersen et al., 1990, *Biochemistry* **29,** 7363-7366; Markussen et al., 1991, *J. Biol. Chem.* **266,** 18814-18818; Schaffer, 1994, *Eur. J. Biochem.* **221,** 1127-1132) and the values of ~1.0 - 5.0 x 10-9 M reported for the hIR +11 ectodomain (Schaefer et al., 1992, *J. Biol. Chem.* **267,** 23393-23402; Whittaker et al., 1994, *Molec. Endocrinol.* **8,** 1521-1527; Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798).

Expression of hIGF-1R ectodomain

Cloning, expression and purification of this protein used elements common to those described for hIR -11 ectodomain (Cosgrove et al., 1995, *Protein Expression and Purification* **6,** 789-798), and resulted in purified product that was recognised by receptor-specific Mabs 17-69, 24-31 and 24-60 (Soos et al., 1992, *J. Biol. Chem.* **267,** 12955-63) and was composed of α and β' subunits of mass similar to those of hIR ectodomain.

Preparation of hIR -11 ectodomain/MFab complexes

A complex of hIR -11 ectodomain and Fab from antibody 83-14 eluted as a symmetrical peak of 460 -500 kDa (Figure 10), as did complexes generated from a mixture of hIR -11 ectodomain with Fab from antibody 18-44 and a mixture of hIR -11 ectodomain with Fab 83-7 (not shown). A co-complex of ectodomain with Fabs from antibodies 18-44 and 83-14 eluted at ~ 620 kDa, as did a co-complex with MFabs 83-14/83-7 and another with MFabs 83-7/18-44 (not shown). A complex of hIR -11 ectodomain with all three MFab derivatives, 18-44, 83-7 and 83-14, eluted at an apparent mass of ~ 710 kDa (Figure 10).

Electron microscopy

Imaging of hIR -11 and hIGF-1R ectodomains

Single-molecule imaging of uncomplexed dimeric hIR -11 ectodomain was carried out under a variety of negative staining conditions, which emphasised different aspects of the structure of the molecular envelope. Images obtained by this investigation are depicted in Figure 11.

The least aggressive or penetrative stain was potassium phosphotungstate (KPT) , which revealed consistent globular particles with very little internal structure other than a suggestion of a division into two parallel bars. Staining with methylamine tungstate also revealed the parallel bar images.

Further investigation using progressively more penetrative, but also potentially more disruptive, stains confirmed the observations above. Staining with uranyl acetate and uranyl formate showed the separation of the parallel bars most clearly, but uranyl acetate showed evidence of disrupting the structure of the particles, i.e. a decrease in the consistency of the particle shape and a tendency for particles to look unravelled or denatured despite having been subjected to chemical cross-linking prior to staining. In areas of thicker stain, parallel bars predominated, whereas in more thinly stained regions, U-shaped particles could be identified, sometimes outnumbering the parallel-bar structures (see Figure 11).

Imaging of hIR -11 ectodomain complexed with 83-7 MFab

This complex was particularly noteworthy for the consistency of the form of the particles, especially under the gentler staining conditions afforded by stains such as KPT and methylamine tungstate. The particles were interpreted as having been restricted in the views they presented, after air-drying on the carbon support film, by the almost diametrically opposite binding of the two Fab arms to the antigen to form a highly elongated complex structure. Under these conditions three distinct views could be recognised (see Figure 11). Two views (interpreted as top-down/bottom-up) show the Fab arms displaced clockwise or anti-clockwise as extensions of the parallel plates with two-fold symmetry. The third view shows an image with the two Fab arms in line roughly through the centre of the receptor on its opposite sides, interpreted as a side projection of binding half-way up the plates.

The use of aggressive uranyl stains operating at lower pHs revealed internal structure of the molecular envelope at the expense of consistency of the particle morphology. For example, staining with uranyl acetate or uranyl

formate showed that parallel bars can be seen in particles in which the Fab arms are displaced either clockwise or anticlockwise but not where the intermediate central or axial position of the two Fab arms is presented in projection. These observations show 83-7 MFab binding roughly half-way up the side-edge of each hIR -11 ectodomain plate. The epitope recognised by Mab 83-7 has been mapped to the cys-rich region, residues 191-297, by analysis of chimeric receptors (Zhang and Roth, 1991, *Proc. Natl. Acad. Sci. USA* **88**, 9858-9862).

Imaging of hIR -11 ectodomain complexed with either 83-14 MFab or 18-44 MFab

Complexes were formed with Fabs from the most insulin-mimetic antibody Mab 83-14. Projections showing the Fab arms bound to and extending out from near the base of the U-shaped particles were identified. A second field of particles showed objects composed of two parallel bars as observed for the undecorated ectodomain, with Fab arms projecting obliquely from diametrically opposite extremities (see Figure 11). Similar but less definitive images were also seen when MFab 18-44 was bound to hIR -11 ectodomain. The epitope for Mab 83-14 is between residues 469-592 (Prigent et al., 1990) in the connecting domain. This domain contains one of the disulphide bonds (Cys524-Cys524) between the two monomers in the IR dimer (Schaffer and Ljungqvist, 1992, *Biochem. Biophys. Res. Commun.* **189,** 650-653). The epitope for Mab 18-44 is a linear epitope, residues 765-770 (Prigent et al., 1990, . *J. Biol. Chem.* **265,** 9970-9977) in the β-chain, near the end of the insert domain (O'Bryan et al., 1991, *Mol. Cell. Biol.* **11,** 5016-5031). The insert domain contains the second disulphide bond connecting the two monomers in the IR dimer (Sparrow et al., 1997, *J. Biol. Chem.*, 272, 29460-29467).

Imaging of hIR -11 ectodomain co-complexed with two different MFabs per monomer

The double complex of hIR -11 ectodomain with MFabs 83-7 and 18-44 was stained with 2% KPT at pH 6.0, and revealed the molecular envelopes. The particle appears complex in shape, and can assume a number of different orientations on the carbon support film, giving rise to a number of different projections in the micrograph. The predominant view is of an asymmetric X-shape (some examples circled). It shows the 83-7 MFab arms bound at opposite ends of the parallel bars with the two 18-44 MFabs

appearing as shorter projections extending out from either side of each ectodomain.

Images of the double complex of hIR -11 ectodomain with 83-7 and 83-14 MFabs gave X-shaped images similar to those seen with the 83-7/18-44 double complex. In contrast the double complex of hIR -11 ectodomain with 18-44 and 83-14 MFabs did not present the characteristic asymmetric X-shapes described above. Instead, the molecular envelope appeared to be elongated in many views, with only an occasional X-shaped projection. While a detailed interpretation of these images would be premature, it is clear that MFabs 18-44 and 83-14, two of the more potent insulin mimetic antibodies (Prigent et al., 1990, *J. Biol. Chem.* **265,** 9970-9977), can bind simultaneously to the receptor.

Imaging of hIR -11 ectodomain co-complexed with three different MFabs per monomer

A field of particles from a micrograph of hIR -11 ectodomain were complexed simultaneously with MFabs 83-7, 83-14 and 18-44. In the thicker stain regions the molecular envelope was X-shaped, and looked very similar to that of the double complexes of hIR -11 ectodomain with either 83-7 and 18-44 or 83-7 and 83-14. However, in the more thinly stained regions particles of greater complexity were visible, and it was possible occasionally to identify that there are in fact more than four MFabs bound to the ectodomain dimer.

The single-molecule imaging of hIR -11 ectodomain presented here suggests a molecular envelope for this dimeric species significantly different from that of any previously published study. However, an unequivocal determination of the molecular envelope even from the present study is not entirely straightforward. A major complicating factor here has been the relative fragility of the expressed ectodomain when exposed to the rigors of electron microscope preparation by negative staining. For example, staining with potassium phosphotungstate (KPT, pH 6.0-7.0) frequently suggested a denaturation of the dimeric molecules, but when appropriate conditions were satisfied, good seemingly interpretable molecular envelope images were achieved; staining with methylamine tungstate (pH ~7.0) supported the best KPT molecular envelope images, but had the suggestion of a swelling of the molecular structure at neutral pH; and the acid-pH stains of uranyl acetate (pH ~4.2) and uranyl formate (pH~3.0), with their ability to penetrate the

ectodomain structure, appeared to illuminate not so much the molecular envelope as the zones of high projected protein density within the dimer.

An amalgam of impressions from these various staining regimens has led to the following interpretation of single-molecule images of these undecorated, or naked, dimers: the predominant dimeric molecular image encountered here has been that of "parallel bars"of projected protein density. This view is so predominant, indeed, that it suggests there is either a single preferred orientation of the molecules on the glow-discharged carbon support film, or that this impression of parallel bars of density may represent a mixture of superficially similar structure projections, with the subtleties of these different projections being masked by the relatively coarse resolution of this single-molecule direct imaging. The impression of parallel bars of projected protein density is particularly predominant in regions of thicker negative stain. A second view of the molecular envelope, appreciably less well represented in regions of thicker stain but predominant in regions of thin staining, is that of 'open' U's, or V's. These two views of hIR -11 ectodomain were supported by the single-molecule imaging of hIGF-1R ectodomain under comparable conditions of negative staining.

If the assumption is made that these two recognisable projected views, that of parallel bars and of open U's/V's, are different views of the same dimeric molecule, an assumption strongly supported by the MFab complex imaging, a coarse model of the molecular envelope can be rationalized. The model structure is roughly that of a cube, composed of two almost-parallel plates of high protein density, separated by a deep cleft of low protein main-chain and side-chain density able to be penetrated by stain, and connected by intermediate stain-excluding density near what is assumed here to be their base (that is, nearest the membrane-anchoring region). The width of the low-density cleft appears to be of the order of 30-35Å, sufficient to accommodate the binding of the insulin molecule of diameter ca. 30Å, although we have no electron microscopical evidence to support insulin-binding in this cleft at this stage.

It has been established through imaging of bound 83-7 MFab that there is a dimeric two-fold axis normal to the membrane surface between these plates of density. Occasionally, dimer images display a relative displacement of the bars of density, interpreted here as a limited capacity for a shearing of the interconnecting zone between the two plates along their

horizontal axis parallel to the membrane; other images show bars skewed from parallel, implying a limited capacity for the plates to rotate independently around the two-fold axis, again via this interconnecting zone. These two observations each suggest a relatively flexible connectivity between the dimer plates in the membrane-proximal region of intermediate protein density, which could possibly contribute to the transmembrane signalling process.

The approximate overall measured dimensions of the ectodomain dimer are 110 x 90 x 120Å, calibrated against the dimensions of imaged influenza neuraminidase heads, known from the solved X-ray structure (Varghese et al., 1983, *Nature* **303**, 35-40). It can be noted that there is a compatibility here between the molecular weights and molecular dimensions of these two molecular species: the compact tetrameric influenza neuraminidase heads of Mr ~200 kDa occupy a volume almost 100 x 100 x 60 Å; the more open dimeric insulin receptor ectodomains of similar Mr ~240 kDa imaged here occupy a volume approximately 110 x 90 x 120 Å , roughly twice that of the neuraminidase heads, accommodating the slightly higher molecular weight and substantial central low-density cleft.

The low-resolution roughly cubic compact structure proposed here differs substantially from the T-shaped model proposed by Christiansen et al. (1991, *Proc. Natl. Acad. Sci. U. S. A.* **88,** 249-252) and Tranum-Jensen et al., (1994, *J. Membrane Biol.* **140,** 215-223) for the whole receptor and the elongated model proposed by Schaefer et al. (1992, *J. Biol. Chem.* **267,** 23393-23402) for soluble ectodomain. Significantly, those previous studies did not provide any convincing independent electron microscopical evidence that their imaged objects were in fact insulin receptor.

In the present study, the identity of the imaged molecules as hIR -11 ectodomain has been confirmed by imaging complexes of the dimer with Fabs of the three well-established conformational Mabs against native hIR, 83-7, 83-14 and 18-44 (Soos et al.,1986, *Biochem. J.* **235,** 199-208; 1989, *Proc. Natl Acad. Sci. USA* **86,** 5217-5221), bound singly and in combination. In all these instances, virtually every particle in the field of view exhibited MFab decoration through binding to conformational epitopes, establishing not only the identity of the imaged particles but also the conformational integrity of the expressed ectodomains. Furthermore, the cleanliness and uniformity of these hIR -11 ectodomain preparations, both naked and decorated, visualised

here by electron microscopy demonstrate their high suitability for X-ray crystallization trials.

The known flexibility of the Fab arms exacerbates image-to-image variability beyond the limited extent already described for the undecorated dimeric ectodomains, complicating any precise interpretation of these antigen-antibody complexes. Such molecular flexibility also renders largely impractical any single-molecule computer image averaging to facilitate image interpretation, progressively more so with the higher order antigen-antibody complexes studied here.

The most readily interpretable of these images, showing least image-to-image variability, are those of 83-7 MFab bound to dimers where, fortuitously, the antigen-antibody complex is constrained in its degrees of rotational freedom on the carbon support film. Many projected images show the two Fab arms in line roughly through the centre of the antigen on its opposite sides, interpreted as a side projection of binding half-way up the plates from their membrane-proximal base. Other sub-sets of images show the two Fab arms still parallel but displaced clockwise or anticlockwise with 2-fold symmetry, each Fab approximating an extension of one of the parallel bars of antigen density, interpreted here as representing top or bottom projections along the 2-fold axis. The third projection, along the axis of the Fab arms, could not be sampled here because of the constraining geometry of this molecular complex. These observations suggest binding of 83-7 MFab roughly half-way up the side-edge of the hIR -11 ectodomain plate. This then allows an initial attempt at spatially mapping the 83-7 MFab epitope, which has been sequence-mapped to residues 191-297 in the cys-rich region of the insulin receptor (Zhang and Roth, 1991, *Proc. Natl. Acad. Sci. USA* **88**, 9858-9862). The spatial separation and relative orientations of the two binding epitopes of Mab 83-7 on the hIR -11 ectodomain dimer as indicated here appear inconsistent with the proposal that Mab 83-7 could bind intramolecularly to hIR (O'Brien et al., 1987, *Biochem J.* **6**, 4003-4010).

Decoration of the ectodomain dimer with 83-7 MFab established that the two plates of high protein-density are arranged with 2-fold symmetry. Decoration with either 83-14 or 18-44 MFab , on the other hand, allowed sampling of the third projection of the ectodomain dimer precluded by 83-7 MFab binding. Significantly, this third view established unequivocally the U-shaped projection of the hIR -11 ectodomain dimer, something which was

only able to be assumed with the undecorated ectodomain images. Further, this projection has allowed a rough spatial mapping close to the base of the U-shaped dimer for the epitopes recognised by 83-14 MFab (residues 469-592, connecting domain) and 18-44 MFab (residues 765-770, b-chain insert domain; exon 11 plus numbering, Prigent et al., 1990, *J. Biol. Chem.* **265,** 9970-9977).

Inherent in the model structure is the implication that, with the two-fold axis aligned normal to the membrane surface, the mouth of the low-density cleft where insulin binding may occur would lie most distant from the transmembrane anchor, whilst the zone of intermediate density connecting the two high-density plates would be in close proximity to the membrane. It follows, in this model, that the L1/cys-rich/L2 domains(Bajaj et al., 1997, *Biochim. Biophys. Acta* **916,** 220-226; Ward et al.,1995, *Proteins: Struct., Funct., Genet.* **22, 141-153**), which comprise much of the insulin-binding region (see Mynarcik et al., 1997, . *J. Biol. Chem.* **272,** 2077-2081), most probably lie in the membrane-distal upper halves of the two plates, whilst the membrane-proximal lower halves contain the connecting domains, the fibronectin-type domains, the insert domains and the interchain disulphide bonds (Schaffer and Ljungqvist, 1992, *Biochem. Biophys. Res. Commun.* **189,** 650-653; Sparrow et al., 1997, *J. Biol. Chem.*, 272, 29460-29467). Such a disposition of domains is supported by the images seen with the single MFab decoration, the 83-7 MFab epitope in the cys-rich region being spatially mapped roughly half-way up the side-edge of the ectodomain plates, and the 83-14 and 18-44 MFab epitopes (connecting domain and β-chain insert domain, respectively) being mapped near the base of the plates. Our preference is for a single a-b¢ monomer to occupy a single plate, although the possibility of a single monomer straddling the two plates of protein density cannot be discounted.

The more complex images involving co-binding of two, and even more so of all three, MFabs to each monomer of the ectodomain dimer are not easily interpretable with respect to relative domain arrangements within the monomer at present, not least of all because of the difficulty of finding conditions of negative staining that will simultaneously maintain the integrity of the Fab binding while highlighting recognisable and reproducible details of the internal structure of the dimeric IR ectodomain.

The data presented here demonstrate the ability of single-molecule imaging to give an initial insight into the topology of multidomain structures such as the ectodomain of hIR, and the value of combining this technique with that of either single or multiple monoclonal Fab attachment per monomer as a potential means of epitope, and domain, mapping of the structure. By imaging Fab complexes of other members of the family, such as hIGF-1R ectodomain, and combining available sequence-mapped epitope information with that presented here, a more comprehensive understanding of domain arrangements within the IR family ectodomains should be forthcoming.

EXAMPLE 5

Structure-Based Design of Ligands for the IGF Receptor as Potential Inhibitors of IGF Binding

The structure of IGF receptor can be considered as a filter or screen to design, or evaluate, potential ligands for the receptor. Those skilled in the art can use a number of well known methods for de novo ligand design, such as GRID, GREEN, HSITE, MCSS, HINT, BUCKETS, CLIX, LUDI, CAVEAT, SPLICE, HOOK, NEWLEAD, PRO_LIGAND, ELANA, LEGEND, GenStar, GrowMol, GROW, GEMINI, GroupBuild, SPROUT, and LEAPFROG, to generate potential agonists or antagonists for IGF-1R. In addition, the IGF-1R structure may be used as a query for database searches for potential ligands. The databases searched may be existing eg ACD, Cambridge Crystallographic, NCI, or virtual. Virtual databases, which contain very large numbers (currently up to 10^{12}) of chemically reasonable structures, may be generated by those skilled in the art using techniques such as DBMaker, ChemSpace, TRIAD and ILIAD.

The IGFR structure contains a number of sites into which putative ligands may bind. Search strategies known to those skilled in the art may be used to identify putative ligands for these sites. Examples of two suitable search strategies are described below:

(i) *Database Search*

The properties of key parts of the putative site may be used as a database search query. For example, the Unity 2.x database software may be used. A flexible 3D search can be run in which a "directed tweak" algorithm is used to find low energy conformations of potential ligands which satisfy the query.

(ii) *De novo design of ligands*

The Leapfrog algorithm as incorporated in the software package, Sybyl version 6.4.2 (Tripos Associates, St Louis), may be used to design potential ligands for IGF-1R sites. The coordinates of residues around the site may be taken from the x-ray structure, hydrogens and charges (Kollman all atom dictionary charges) added. From the size, shape and properties of the site, a number of potential ligands may be proposed. Leapfrog may be used to optimize the conformation of ligands and position on the site, to rank the likely strength of binding interactions with IGF-1R, and to suggest modifications to the structures which would have enhanced binding.

It is also possible to design ligands capable of interacting with more than one site. One way in which this may be done is by attaching flexible linkers to ligands designed for specific sites so as to join them. The linkers may be attached in such a way that they do not disrupt the binding to individual sites.

All references cited above are incorporated herein in their entirety by reference.

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

Claims:

1. A method of designing a compound able to bind to a molecule of the insulin receptor family and to modulate an activity mediated by the molecule, including the step of assessing the stereochemical complementarity between the compound and the receptor site of the molecule, wherein the receptor site includes:

(a) amino acids 1 to 462 of the receptor for IGF-1, having the atomic coordinates substantially as shown in Figure 1;

(b) a subset of said amino acids, or;

(c) amino acids present in the amino acid sequence of a member of the insulin receptor family, which form an equivalent three-dimensional structure to that of the receptor molecule as depicted in Figure 1.

2. A method according to claim 1, in which the compound is selected or modified from a known compound identified from a database.

3. A method according to claim 1, in which the compound is designed so as to complement the structure of the receptor molecule as depicted in Figure 1.

4. A method according to any one of claims 1 to 3, in which the compound has structural regions able to make close contact with amino acid residues at the surface of the receptor site lining the groove, as depicted in Figure 2.

5. A method according to any one of claims 1 to 4, in which the compound has a stereochemistry such that it can interact with both the L1 and L2 domains of the receptor site.

6. A method according to any one of claims 1 to 4, in which the compound has a stereochemistry such that it can interact with the L1 domain of a first monomer of the receptor homodimer, and with the L2 domain of the other monomer of the receptor homodimer.

7. A method according to any one of claims 1 to 4, in which the interaction of the compound with the receptor site alters the position of at least one of the

L1, L2 or cysteine-rich domains of the receptor molecule relative to the position of at least one of the other of said domains.

8. A method according to claim 7, in which the compound interacts with the β sheet of the L1 domain of the receptor molecule, thereby causing an alteration in the position of the L1 domain relative to the position of the cysteine-rich domain or of the L2 domain.

9. A method according to claim 7, in which the compound interacts with the receptor site in the region of the interface between the L1 domain an the cysteine-rich domain of the receptor molecule, thereby causing the L1 domain and the cysteine-rich domain to move away from each other.

10. A method according to claim 7, in which the compound interacts with the hinge region between the L2 domain and the cysteine-rich domain of the receptor molecule, thereby causing an alteration in the positions of the L2 domain and the cysteine-rich domain relative to each other.

11. A method according to any one of claims 1 to 10, in which the stereochemical complementarity between the compound and the receptor site is such that the compound has a K_b for the receptor side of less than 10^{-6}M.

12. A method according to claim 11, in which the K_b is less than 10^{-8}M.

13. A method according to any one of claims 1 to 12, in which the compound has the ability to increase an activity mediated by the receptor molecule.

14. A method according to any one of claims 1 to 12, in which the compound has the ability to decrease an activity mediated by the receptor molecule.

15. A method according to claim 14, in which the stereochemical interaction between the compound and the receptor site is adapted to prevent the binding of a natural ligand of the receptor molecule to the receptor site.

16. A method according to claim 14 or claim 15, in which the compound has a K_1 of less than 10^{-6}M.

17. A method according to claim 16, in which the compound has a K_1 of less than 10^{-8}M.

18. A method according to claim 17, in which the compound has a K_1 of less than 10^{-9}M.

19. A method according to any one of claims 1 to 18, in which the receptor is the IGF-1R.

20. A method according to any one of claims 1 to 18, in which the receptor is the insulin receptor.

21. A computer-assisted method for identifying potential compounds able to bind to a molecule of the insulin receptor family and to modulate an activity mediated by the molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data comprising the atomic coordinates of the IGF-1R molecule as shown in Figure 1, or a subset thereof;

(b) generating, using computer methods, a set of atomic coordinates of a structure that possesses stereochemical complementarity to the atomic coordinates of the IGF-1R site as shown in Figure 1, or a subset thereof, thereby generating a criteria data set;

(c) comparing, using the processor, the criteria data set to a computer database of chemical structures;

(d) selecting from the database, using computer methods, chemical structures which are structurally similar to a portion of said criteria data set; and

(e) outputting, to the output device, the selected chemical structures which are similar to a portion of the criteria data set.

22. A computer-assisted method according to claim 21, in which the method is used to identify potential compounds which have the ability to decrease an activity mediated by the receptor.

23. A computer-assisted method according to claim 21 or claim 22, which further includes the step of selecting one or more chemical structures from step (e) which interact with the receptor site of the molecule in a manner which prevents the binding of natural ligands to the receptor site.

24. A computer-assisted method according to any one of claims 21 to 23, which further includes the step of obtaining a compound with a chemical structure selected in steps (d) and (e), and testing the compound for the ability to decrease an activity mediated by the receptor.

25. A computer-assisted method according to claim 21, in which the method is used to identify potential compounds which have the ability to increase an activity mediated by the receptor molecule.

26. A computer-assisted method according to claim 25, further including the step of obtaining a molecule with a chemical structure selected in steps (d) and (e), and testing the compound for the ability to increase an activity mediated by the receptor.

27. A computer-assisted method according to any one of claims 21 to 26, in which the receptor is the IGF-1R.

28. A computer-assisted method according to any one of claims 21 to 26, in which the receptor is the insulin receptor.

29. A method of screening of a putative compound having the ability to modulate the activity of a receptor of the insulin receptor family, including the steps of identifying a putative compound by a method according to any one of claims 1 to 29, and testing the compound for the ability to increase or decrease an activity mediated by the receptor.

30. A method according to claim 29, in which the test is carried out *in vitro*.

31. A method according to claim 29, in which the test is a high throughput assay.

32. A method according to claim 29, in which the test is carried out *in vivo*.

33. A method according to claim 30, in which the test is carried out *in vivo*.

Figure 1

```
ATOM      1  CB  GLU     1      55.907  11.986  66.300  1.00 59.11      AAAA C
ATOM      2  CG  GLU     1      56.138  11.019  65.162  1.00 78.17      AAAA C
ATOM      3  CD  GLU     1      57.382  11.319  64.321  1.00 85.10      AAAA C
ATOM      4  OE1 GLU     1      58.404  10.754  64.796  1.00 86.18      AAAA O
ATOM      5  OE2 GLU     1      57.424  12.013  63.270  1.00 78.70      AAAA O
ATOM      6  C   GLU     1      53.508  12.557  66.350  1.00 48.46      AAAA C
ATOM      7  O   GLU     1      52.685  11.863  65.784  1.00 51.27      AAAA O
ATOM     10  N   GLU     1      54.256  10.338  67.159  1.00 61.64      AAAA N
ATOM     12  CA  GLU     1      54.602  11.778  67.081  1.00 54.77      AAAA C
ATOM     13  N   ILE     2      53.608  13.860  66.375  1.00 37.66      AAAA N
ATOM     15  CA  ILE     2      52.768  14.699  65.604  1.00 40.87      AAAA C
ATOM     16  CB  ILE     2      52.925  16.122  66.160  1.00 41.97      AAAA C
ATOM     17  CG2 ILE     2      52.036  17.122  65.484  1.00 38.50      AAAA C
ATOM     18  CG1 ILE     2      52.560  16.006  67.663  1.00 46.58      AAAA C
ATOM     19  CD1 ILE     2      53.150  17.176  68.498  1.00 32.29      AAAA C
ATOM     20  C   ILE     2      53.122  14.711  64.139  1.00 46.47      AAAA C
ATOM     21  O   ILE     2      54.258  15.029  63.852  1.00 51.66      AAAA O
ATOM     22  N   CYS     3      52.235  14.409  63.196  1.00 49.61      AAAA N
ATOM     24  CA  CYS     3      52.435  14.677  61.773  1.00 38.93      AAAA C
ATOM     25  C   CYS     3      51.429  15.708  61.302  1.00 42.06      AAAA C
ATOM     26  O   CYS     3      50.290  15.521  61.690  1.00 42.37      AAAA O
ATOM     27  CB  CYS     3      52.159  13.415  60.999  1.00 35.66      AAAA C
ATOM     28  SG  CYS     3      53.019  12.004  61.674  1.00 36.98      AAAA S
ATOM     29  N   GLY     4      51.851  16.709  60.580  1.00 42.39      AAAA N
ATOM     31  CA  GLY     4      50.973  17.718  60.003  1.00 47.71      AAAA C
ATOM     32  C   GLY     4      51.703  18.407  58.869  1.00 48.23      AAAA C
ATOM     33  O   GLY     4      52.916  18.345  58.884  1.00 55.36      AAAA O
ATOM     34  N   PRO     5      51.056  19.212  58.048  1.00 49.63      AAAA N
ATOM     35  CD  PRO     5      51.637  19.947  56.860  1.00 45.28      AAAA C
ATOM     36  CA  PRO     5      49.605  19.341  58.083  1.00 41.57      AAAA C
ATOM     37  CB  PRO     5      49.397  20.703  57.474  1.00 44.30      AAAA C
ATOM     38  CG  PRO     5      50.632  21.036  56.683  1.00 46.43      AAAA C
ATOM     39  C   PRO     5      48.932  18.217  57.354  1.00 36.40      AAAA C
ATOM     40  O   PRO     5      49.403  17.094  57.396  1.00 43.35      AAAA O
ATOM     41  N   GLY     6      47.787  18.438  56.795  1.00 39.15      AAAA N
ATOM     43  CA  GLY     6      46.896  17.336  56.350  1.00 39.24      AAAA C
ATOM     44  C   GLY     6      47.710  16.365  55.529  1.00 33.68      AAAA C
ATOM     45  O   GLY     6      48.510  16.863  54.753  1.00 36.00      AAAA O
ATOM     46  N   ILE     7      47.586  15.111  55.788  1.00 35.70      AAAA N
ATOM     48  CA  ILE     7      48.307  14.053  55.141  1.00 37.65      AAAA C
ATOM     49  CB  ILE     7      48.556  12.797  55.933  1.00 36.31      AAAA C
ATOM     50  CG2 ILE     7      49.043  11.700  54.988  1.00 34.67      AAAA C
ATOM     51  CG1 ILE     7      49.561  12.857  57.067  1.00 39.34      AAAA C
ATOM     52  CD1 ILE     7      49.678  14.249  57.668  1.00 40.22      AAAA C
ATOM     53  C   ILE     7      47.338  13.762  53.977  1.00 45.00      AAAA C
ATOM     54  O   ILE     7      46.150  13.843  54.195  1.00 51.52      AAAA O
ATOM     55  N   ASP     8      47.767  13.631  52.751  1.00 45.60      AAAA N
ATOM     57  CA  ASP     8      46.938  13.283  51.631  1.00 44.05      AAAA C
ATOM     58  CB  ASP     8      47.003  14.469  50.651  1.00 44.21      AAAA C
ATOM     59  CG  ASP     8      45.909  14.379  49.600  1.00 43.48      AAAA C
ATOM     60  OD1 ASP     8      45.660  13.262  49.096  1.00 51.77      AAAA O
ATOM     61  OD2 ASP     8      45.253  15.374  49.251  1.00 46.84      AAAA O
ATOM     62  C   ASP     8      47.428  12.000  50.992  1.00 42.16      AAAA C
ATOM     63  O   ASP     8      48.423  12.143  50.330  1.00 48.50      AAAA O
ATOM     64  N   ILE     9      47.096  10.817  51.321  1.00 42.76      AAAA N
ATOM     66  CA  ILE     9      47.441   9.505  50.939  1.00 44.05      AAAA C
ATOM     67  CB  ILE     9      47.212   8.483  52.077  1.00 40.82      AAAA C
ATOM     68  CG2 ILE     9      47.669   7.085  51.653  1.00 36.35      AAAA C
ATOM     69  CG1 ILE     9      47.888   8.917  53.364  1.00 41.17      AAAA C
ATOM     70  CD1 ILE     9      49.376   8.947  53.286  1.00 43.78      AAAA C
ATOM     71  C   ILE     9      46.530   9.137  49.794  1.00 51.48      AAAA C
ATOM     72  O   ILE     9      45.338   9.420  49.832  1.00 63.05      AAAA O
ATOM     73  N   ARG    10      47.004   8.417  48.812  1.00 54.87      AAAA N
ATOM     75  CA  ARG    10      46.283   8.089  47.600  1.00 54.17      AAAA C
ATOM     76  CB  ARG    10      45.703   9.358  47.023  1.00 48.54      AAAA C
ATOM     77  CG  ARG    10      46.361  10.169  45.952  1.00 46.55      AAAA C
ATOM     78  CD  ARG    10      46.002  11.635  46.264  1.00 52.63      AAAA C
ATOM     79  NE  ARG    10      45.082  12.226  45.284  1.00 59.27      AAAA N
ATOM     81  CZ  ARG    10      44.269  13.262  45.498  1.00 56.22      AAAA C
ATOM     82  NH1 ARG    10      44.153  13.891  46.666  1.00 55.14      AAAA N
ATOM     85  NH2 ARG    10      43.455  13.803  44.602  1.00 52.29      AAAA N
ATOM     88  C   ARG    10      47.019   7.373  46.492  1.00 57.23      AAAA C
ATOM     89  O   ARG    10      48.240   7.288  46.281  1.00 56.32      AAAA O
ATOM     90  N   ASN    11      46.248   6.654  45.629  1.00 57.23      AAAA N
ATOM     92  CA  ASN    11      46.800   5.917  44.494  1.00 50.73      AAAA C
ATOM     93  CB  ASN    11      47.704   6.798  43.671  1.00 44.65      AAAA C
ATOM     94  CG  ASN    11      46.878   7.732  42.829  1.00 50.72      AAAA C
ATOM     95  OD1 ASN    11      45.749   7.451  42.403  1.00 72.59      AAAA O
ATOM     96  ND2 ASN    11      47.499   8.869  42.587  1.00 54.38      AAAA N
ATOM     99  C   ASN    11      47.635   4.736  44.915  1.00 53.07      AAAA C
ATOM    100  O   ASN    11      47.303   3.701  44.347  1.00 51.95      AAAA O
ATOM    101  N   ASP    12      48.566   4.822  45.878  1.00 50.96      AAAA N
ATOM    103  CA  ASP    12      49.204   3.570  46.263  1.00 55.44      AAAA C
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ATOM    104  CB  ASP    12      50.668   3.568  45.758  1.00 66.47      AAAA C
ATOM    105  CG  ASP    12      50.879   4.026  44.314  1.00 68.25      AAAA C
ATOM    106  OD1 ASP    12      50.441   3.185  43.457  1.00 58.31      AAAA O
ATOM    107  OD2 ASP    12      51.391   5.120  43.989  1.00 70.56      AAAA O
ATOM    108  C   ASP    12      49.061   3.322  47.758  1.00 59.23      AAAA C
ATOM    109  O   ASP    12      49.687   3.849  48.711  1.00 59.65      AAAA O
ATOM    110  N   TYR    13      48.411   2.187  48.036  1.00 59.64      AAAA N
ATOM    112  CA  TYR    13      48.328   1.672  49.397  1.00 64.06      AAAA C
ATOM    113  CB  TYR    13      47.968   0.196  49.409  1.00 64.56      AAAA C
ATOM    114  CG  TYR    13      47.467  -0.357  50.721  1.00 69.18      AAAA C
ATOM    115  CD1 TYR    13      46.216  -0.024  51.248  1.00 72.71      AAAA C
ATOM    116  CE1 TYR    13      45.746  -0.541  52.450  1.00 71.51      AAAA C
ATOM    117  CD2 TYR    13      48.233  -1.247  51.457  1.00 70.36      AAAA C
ATOM    118  CE2 TYR    13      47.788  -1.778  52.661  1.00 71.64      AAAA C
ATOM    119  CZ  TYR    13      46.542  -1.420  53.160  1.00 71.31      AAAA C
ATOM    120  OH  TYR    13      46.144  -1.977  54.358  1.00 63.25      AAAA O
ATOM    122  C   TYR    13      49.622   1.839  50.198  1.00 65.99      AAAA C
ATOM    123  O   TYR    13      49.621   2.321  51.354  1.00 65.01      AAAA O
ATOM    124  N   GLN    14      50.786   1.541  49.594  1.00 63.51      AAAA N
ATOM    126  CA  GLN    14      52.078   1.681  50.218  1.00 63.51      AAAA C
ATOM    127  CB  GLN    14      53.174   1.318  49.219  1.00 68.37      AAAA C
ATOM    128  CG  GLN    14      52.863  -0.078  48.686  1.00 84.62      AAAA C
ATOM    129  CD  GLN    14      53.990  -0.515  47.754  1.00 92.28      AAAA C
ATOM    130  OE1 GLN    14      53.945  -0.161  46.573  1.00 94.82      AAAA O
ATOM    131  NE2 GLN    14      54.920  -1.254  48.361  1.00 98.03      AAAA N
ATOM    134  C   GLN    14      52.434   3.058  50.753  1.00 61.62      AAAA C
ATOM    135  O   GLN    14      53.266   3.292  51.644  1.00 62.09      AAAA O
ATOM    136  N   LEU    15      51.628   4.038  50.349  1.00 57.02      AAAA N
ATOM    138  CA  LEU    15      51.724   5.399  50.831  1.00 51.71      AAAA C
ATOM    139  CB  LEU    15      50.861   6.220  49.911  1.00 43.75      AAAA C
ATOM    140  CG  LEU    15      51.566   6.605  48.648  1.00 59.65      AAAA C
ATOM    141  CD  LEU    15      51.554   8.105  48.428  1.00 72.96      AAAA C
ATOM    142  OE1 LEU    15      51.168   9.005  49.184  1.00 80.58      AAAA O
ATOM    143  NE2 LEU    15      52.016   8.378  47.211  1.00 74.17      AAAA N
ATOM    146  C   LEU    15      51.219   5.530  52.258  1.00 50.15      AAAA C
ATOM    147  O   LEU    15      51.576   6.500  52.940  1.00 48.04      AAAA O
ATOM    148  N   LEU    16      50.440   4.535  52.688  1.00 46.22      AAAA N
ATOM    150  CA  LEU    16      49.913   4.449  54.019  1.00 45.52      AAAA C
ATOM    151  CB  LEU    16      48.950   3.295  54.159  1.00 37.73      AAAA C
ATOM    152  CG  LEU    16      47.502   3.425  53.707  1.00 41.40      AAAA C
ATOM    153  CD1 LEU    16      46.837   2.063  53.790  1.00 42.43      AAAA C
ATOM    154  CD2 LEU    16      46.687   4.424  54.545  1.00 35.93      AAAA C
ATOM    155  C   LEU    16      51.042   4.280  55.039  1.00 51.52      AAAA C
ATOM    156  O   LEU    16      50.913   4.601  56.235  1.00 52.53      AAAA O
ATOM    157  N   LYS    17      52.252   3.936  54.560  1.00 51.01      AAAA N
ATOM    159  CA  LYS    17      53.422   3.914  55.404  1.00 50.73      AAAA C
ATOM    160  CB  LYS    17      54.609   3.252  54.737  1.00 56.10      AAAA C
ATOM    161  CG  LYS    17      54.539   1.733  54.831  1.00 62.40      AAAA C
ATOM    162  CD  LYS    17      54.768   1.278  53.387  1.00 63.85      AAAA C
ATOM    163  CE  LYS    17      55.316  -0.141  53.426  1.00 68.40      AAAA C
ATOM    164  NZ  LYS    17      56.537  -0.225  52.554  1.00 73.83      AAAA N
ATOM    168  C   LYS    17      53.944   5.270  55.852  1.00 44.78      AAAA C
ATOM    169  O   LYS    17      54.492   5.262  56.933  1.00 39.39      AAAA O
ATOM    170  N   ARG    18      53.524   6.344  55.201  1.00 41.15      AAAA N
ATOM    172  CA  ARG    18      53.827   7.673  55.676  1.00 43.01      AAAA C
ATOM    173  CB  ARG    18      53.250   8.702  54.704  1.00 43.97      AAAA C
ATOM    174  CG  ARG    18      53.888   8.764  53.333  1.00 53.60      AAAA C
ATOM    175  CD  ARG    18      52.964   9.362  52.269  1.00 60.34      AAAA C
ATOM    176  NE  ARG    18      52.528  10.703  52.650  1.00 50.00      AAAA N
ATOM    178  CZ  ARG    18      51.628  11.444  52.021  1.00 48.86      AAAA C
ATOM    179  NH1 ARG    18      51.068  10.941  50.943  1.00 47.96      AAAA N
ATOM    182  NH2 ARG    18      51.377  12.656  52.555  1.00 43.72      AAAA N
ATOM    185  C   ARG    18      53.268   7.924  57.077  1.00 44.03      AAAA C
ATOM    186  O   ARG    18      53.402   9.010  57.644  1.00 45.53      AAAA O
ATOM    187  N   LEU    19      52.445   7.069  57.632  1.00 46.36      AAAA N
ATOM    189  CA  LEU    19      51.653   7.282  58.794  1.00 50.25      AAAA C
ATOM    190  CB  LEU    19      50.186   6.924  58.674  1.00 50.83      AAAA C
ATOM    191  CG  LEU    19      49.202   7.371  57.608  1.00 46.43      AAAA C
ATOM    192  CD1 LEU    19      47.846   6.743  57.852  1.00 22.57      AAAA C
ATOM    193  CD2 LEU    19      49.018   8.866  57.495  1.00 45.88      AAAA C
ATOM    194  C   LEU    19      52.210   6.428  59.912  1.00 49.87      AAAA C
ATOM    195  O   LEU    19      51.970   6.810  61.030  1.00 51.54      AAAA O
ATOM    196  N   GLU    20      53.270   5.708  59.652  1.00 49.35      AAAA N
ATOM    198  CA  GLU    20      53.819   4.833  60.679  1.00 49.60      AAAA C
ATOM    199  CB  GLU    20      54.876   3.960  59.982  1.00 57.91      AAAA C
ATOM    200  CG  GLU    20      55.893   4.840  59.272  1.00 70.16      AAAA C
ATOM    201  CD  GLU    20      57.095   4.077  58.757  1.00 69.35      AAAA C
ATOM    202  OE1 GLU    20      58.123   4.795  58.722  1.00 71.38      AAAA O
ATOM    203  OE2 GLU    20      56.993   2.885  58.420  1.00 72.84      AAAA O
ATOM    204  C   GLU    20      54.310   5.417  61.989  1.00 43.55      AAAA C
ATOM    205  O   GLU    20      54.301   4.652  62.937  1.00 40.01      AAAA O
ATOM    206  N   ASN    21      54.633   6.659  62.207  1.00 41.06      AAAA N
ATOM    208  CA  ASN    21      55.054   7.204  63.454  1.00 47.17      AAAA C
ATOM    209  C   ASN    21      54.066   8.141  64.108  1.00 49.76      AAAA C
ATOM    210  O   ASN    21      54.228   8.456  65.303  1.00 48.10      AAAA O
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ATOM    211  CB  ASN    21      56.379   8.003  63.290  1.00 59.11      AAAA C
ATOM    212  CG  ASN    21      57.413   7.051  62.796  1.00 68.38      AAAA C
ATOM    213  OD1 ASN    21      57.499   5.855  63.122  1.00 58.51      AAAA O
ATOM    214  ND2 ASN    21      58.348   7.469  61.890  1.00 77.90      AAAA N
ATOM    216  N   CYS    22      53.129   8.711  63.351  1.00 47.44      AAAA N
ATOM    218  CA  CYS    22      52.107   9.614  63.879  1.00 42.99      AAAA C
ATOM    219  C   CYS    22      51.215   9.089  65.021  1.00 40.43      AAAA C
ATOM    220  O   CYS    22      50.750   7.923  65.069  1.00 36.07      AAAA O
ATOM    221  CB  CYS    22      51.182   9.921  62.690  1.00 44.82      AAAA C
ATOM    222  SG  CYS    22      52.076  10.328  61.148  1.00 39.51      AAAA S
ATOM    223  N   THR    23      51.287   9.801  66.137  1.00 36.24      AAAA N
ATOM    225  CA  THR    23      50.339   9.482  67.204  1.00 43.51      AAAA C
ATOM    226  CB  THR    23      50.944   9.481  68.593  1.00 41.38      AAAA C
ATOM    227  OG1 THR    23      51.410  10.843  68.822  1.00 51.21      AAAA O
ATOM    229  CG2 THR    23      52.110   8.571  68.838  1.00 33.83      AAAA C
ATOM    230  C   THR    23      49.250  10.599  67.116  1.00 44.55      AAAA C
ATOM    231  O   THR    23      48.085  10.414  67.481  1.00 45.95      AAAA O
ATOM    232  N   VAL    24      49.646  11.797  66.689  1.00 33.03      AAAA N
ATOM    234  CA  VAL    24      48.732  12.855  66.442  1.00 35.29      AAAA C
ATOM    235  CB  VAL    24      48.925  13.979  67.456  1.00 30.60      AAAA C
ATOM    236  CG1 VAL    24      48.056  15.157  67.082  1.00 27.21      AAAA C
ATOM    237  CG2 VAL    24      48.656  13.566  68.886  1.00 25.37      AAAA C
ATOM    238  C   VAL    24      48.895  13.447  65.043  1.00 41.52      AAAA C
ATOM    239  O   VAL    24      49.987  13.963  64.791  1.00 44.40      AAAA O
ATOM    240  N   ILE    25      47.855  13.450  64.203  1.00 40.13      AAAA N
ATOM    242  CA  ILE    25      47.908  14.094  62.882  1.00 32.05      AAAA C
ATOM    243  CB  ILE    25      47.113  13.299  61.853  1.00 25.85      AAAA C
ATOM    244  CG2 ILE    25      47.027  14.039  60.542  1.00 18.73      AAAA C
ATOM    245  CG1 ILE    25      47.677  11.896  61.705  1.00 29.80      AAAA C
ATOM    246  CD1 ILE    25      47.169  11.155  60.471  1.00 27.41      AAAA C
ATOM    247  C   ILE    25      47.397  15.490  62.941  1.00 32.92      AAAA C
ATOM    248  O   ILE    25      46.223  15.776  63.213  1.00 40.91      AAAA O
ATOM    249  N   GLU    26      48.264  16.472  63.042  1.00 36.60      AAAA N
ATOM    251  CA  GLU    26      47.832  17.847  63.226  1.00 29.24      AAAA C
ATOM    252  CB  GLU    26      48.875  18.703  63.856  1.00 29.92      AAAA C
ATOM    253  CG  GLU    26      48.490  20.144  64.116  1.00 38.06      AAAA C
ATOM    254  CD  GLU    26      49.561  20.762  65.013  1.00 37.39      AAAA C
ATOM    255  OE1 GLU    26      50.654  20.937  64.489  1.00 41.56      AAAA O
ATOM    256  OE2 GLU    26      49.571  21.175  66.182  1.00 49.16      AAAA O
ATOM    257  C   GLU    26      47.413  18.376  61.869  1.00 37.79      AAAA C
ATOM    258  O   GLU    26      48.161  19.069  61.181  1.00 39.68      AAAA O
ATOM    259  N   GLY    27      46.117  18.104  61.582  1.00 37.28      AAAA N
ATOM    261  CA  GLY    27      45.498  18.503  60.320  1.00 31.17      AAAA C
ATOM    262  C   GLY    27      44.531  17.400  59.893  1.00 33.72      AAAA C
ATOM    263  O   GLY    27      43.988  16.715  60.775  1.00 33.29      AAAA O
ATOM    264  N   TYR    28      44.304  17.209  58.604  1.00 29.24      AAAA N
ATOM    266  CA  TYR    28      43.318  16.189  58.253  1.00 28.93      AAAA C
ATOM    267  CB  TYR    28      42.403  16.794  57.217  1.00 31.53      AAAA C
ATOM    268  CG  TYR    28      43.058  17.256  55.962  1.00 31.78      AAAA C
ATOM    269  CD1 TYR    28      43.704  16.355  55.116  1.00 36.07      AAAA C
ATOM    270  CE1 TYR    28      44.361  16.706  53.967  1.00 28.91      AAAA C
ATOM    271  CD2 TYR    28      43.130  18.572  55.606  1.00 30.98      AAAA C
ATOM    272  CE2 TYR    28      43.769  18.972  54.428  1.00 28.77      AAAA C
ATOM    273  CZ  TYR    28      44.367  18.021  53.652  1.00 31.53      AAAA C
ATOM    274  OH  TYR    28      44.971  18.425  52.464  1.00 44.74      AAAA O
ATOM    276  C   TYR    28      43.953  14.946  57.697  1.00 29.23      AAAA C
ATOM    277  O   TYR    28      45.119  15.147  57.383  1.00 35.58      AAAA O
ATOM    278  N   LEU    29      43.250  13.900  57.445  1.00 26.63      AAAA N
ATOM    280  CA  LEU    29      43.764  12.730  56.803  1.00 29.83      AAAA C
ATOM    281  CB  LEU    29      43.830  11.611  57.856  1.00 27.09      AAAA C
ATOM    282  CG  LEU    29      44.212  10.258  57.242  1.00 31.90      AAAA C
ATOM    283  CD1 LEU    29      45.538  10.396  56.469  1.00 35.03      AAAA C
ATOM    284  CD2 LEU    29      44.551   9.203  58.290  1.00 25.05      AAAA C
ATOM    285  C   LEU    29      42.897  12.342  55.616  1.00 33.84      AAAA C
ATOM    286  O   LEU    29      41.689  12.165  55.806  1.00 43.29      AAAA O
ATOM    287  N   HIS    30      43.389  12.285  54.395  1.00 35.95      AAAA N
ATOM    289  CA  HIS    30      42.681  11.891  53.197  1.00 34.92      AAAA C
ATOM    290  CB  HIS    30      42.893  12.801  52.027  1.00 32.85      AAAA C
ATOM    291  CG  HIS    30      42.372  14.155  52.046  1.00 25.08      AAAA C
ATOM    292  CD2 HIS    30      41.519  14.753  52.907  1.00 40.88      AAAA C
ATOM    293  ND1 HIS    30      42.717  15.120  51.128  1.00 33.66      AAAA N
ATOM    295  CE1 HIS    30      42.080  16.281  51.444  1.00 31.33      AAAA C
ATOM    296  NE2 HIS    30      41.329  16.093  52.539  1.00 37.27      AAAA N
ATOM    298  C   HIS    30      43.173  10.538  52.714  1.00 37.68      AAAA C
ATOM    299  O   HIS    30      44.357  10.388  52.541  1.00 38.70      AAAA O
ATOM    300  N   ILE    31      42.308   9.542  52.584  1.00 40.02      AAAA N
ATOM    302  CA  ILE    31      42.750   8.271  51.992  1.00 39.47      AAAA C
ATOM    303  CB  ILE    31      42.668   7.204  53.063  1.00 37.95      AAAA C
ATOM    304  CG2 ILE    31      43.161   5.830  52.651  1.00 23.86      AAAA C
ATOM    305  CG1 ILE    31      43.481   7.555  54.335  1.00 41.66      AAAA C
ATOM    306  CD1 ILE    31      43.170   6.575  55.473  1.00 28.22      AAAA C
ATOM    307  C   ILE    31      41.884   8.044  50.755  1.00 46.52      AAAA C
ATOM    308  O   ILE    31      40.753   7.589  50.827  1.00 43.56      AAAA O
ATOM    309  N   LEU    32      42.314   8.489  49.556  1.00 49.89      AAAA N
ATOM    311  CA  LEU    32      41.484   8.235  48.380  1.00 49.77      AAAA C
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ATOM    312  CB  LEU    32      41.127   9.515  47.603  1.00 47.49      AAAA C
ATOM    313  CG  LEU    32      42.091  10.688  47.562  1.00 45.33      AAAA C
ATOM    314  CD1 LEU    32      41.517  11.812  46.673  1.00 35.77      AAAA C
ATOM    315  CD2 LEU    32      42.371  11.229  48.960  1.00 49.18      AAAA C
ATOM    316  C   LEU    32      42.136   7.296  47.353  1.00 51.00      AAAA C
ATOM    317  O   LEU    32      43.338   7.370  47.186  1.00 41.36      AAAA O
ATOM    318  N   LEU    33      41.270   6.722  46.497  1.00 50.74      AAAA N
ATOM    320  CA  LEU    33      41.602   6.175  45.197  1.00 49.92      AAAA C
ATOM    321  CB  LEU    33      42.091   7.262  44.182  1.00 34.83      AAAA C
ATOM    322  CG  LEU    33      41.233   8.537  44.164  1.00 33.92      AAAA C
ATOM    323  CD1 LEU    33      41.892   9.587  43.298  1.00 37.49      AAAA C
ATOM    324  CD2 LEU    33      39.823   8.313  43.644  1.00 33.01      AAAA C
ATOM    325  C   LEU    33      42.618   5.073  45.287  1.00 48.35      AAAA C
ATOM    326  O   LEU    33      43.580   5.077  44.538  1.00 54.14      AAAA O
ATOM    327  N   ILE    34      42.543   4.212  46.254  1.00 47.61      AAAA N
ATOM    329  CA  ILE    34      43.523   3.184  46.540  1.00 51.70      AAAA C
ATOM    330  CB  ILE    34      44.101   3.346  47.963  1.00 57.98      AAAA C
ATOM    331  CG2 ILE    34      44.538   2.043  48.600  1.00 48.98      AAAA C
ATOM    332  CG1 ILE    34      45.267   4.371  47.967  1.00 46.70      AAAA C
ATOM    333  CD1 ILE    34      45.561   4.704  49.439  1.00 66.47      AAAA C
ATOM    334  C   ILE    34      42.829   1.844  46.408  1.00 59.85      AAAA C
ATOM    335  O   ILE    34      41.726   1.531  46.856  1.00 60.11      AAAA O
ATOM    336  N   SER    35      43.622   0.833  46.013  1.00 67.79      AAAA N
ATOM    338  CA  SER    35      43.048  -0.511  45.922  1.00 68.80      AAAA C
ATOM    339  CB  SER    35      42.767  -0.882  44.469  1.00 64.16      AAAA C
ATOM    340  OG  SER    35      41.731  -1.846  44.498  1.00 75.76      AAAA O
ATOM    342  C   SER    35      43.928  -1.564  46.537  1.00 70.73      AAAA C
ATOM    343  O   SER    35      44.885  -1.954  45.909  1.00 73.65      AAAA O
ATOM    344  N   LYS    36      43.687  -2.017  47.740  1.00 74.75      AAAA N
ATOM    346  CA  LYS    36      44.465  -3.014  48.421  1.00 76.09      AAAA C
ATOM    347  CB  LYS    36      44.046  -3.131  49.885  1.00 81.22      AAAA C
ATOM    348  CG  LYS    36      45.147  -3.654  50.775  1.00 78.87      AAAA C
ATOM    349  CD  LYS    36      44.693  -4.575  51.887  1.00 81.39      AAAA C
ATOM    350  CE  LYS    36      44.890  -6.025  51.492  1.00 89.38      AAAA C
ATOM    351  NZ  LYS    36      44.371  -6.989  52.506  1.00 91.63      AAAA N
ATOM    355  C   LYS    36      44.252  -4.362  47.753  1.00 81.41      AAAA C
ATOM    356  O   LYS    36      43.145  -4.772  47.451  1.00 78.20      AAAA O
ATOM    357  N   ALA    37      45.371  -5.080  47.615  1.00 88.27      AAAA N
ATOM    359  CA  ALA    37      45.361  -6.396  46.986  1.00 90.10      AAAA C
ATOM    360  CB  ALA    37      46.700  -6.655  46.327  1.00 95.49      AAAA C
ATOM    361  C   ALA    37      45.011  -7.473  47.995  1.00 92.36      AAAA C
ATOM    362  O   ALA    37      45.668  -7.627  49.012  1.00 92.35      AAAA O
ATOM    363  N   SER    38      44.031  -8.301  47.622  1.00 94.31      AAAA N
ATOM    365  CA  SER    38      43.528  -9.352  48.484  1.00 95.70      AAAA C
ATOM    366  CB  SER    38      42.405 -10.164  47.858  1.00 97.44      AAAA C
ATOM    367  OG  SER    38      42.061 -11.176  48.814  1.00103.48      AAAA O
ATOM    369  C   SER    38      44.702 -10.263  48.821  1.00 96.87      AAAA C
ATOM    370  O   SER    38      44.761 -10.778  49.924  1.00 98.06      AAAA O
ATOM    371  N   ASP    39      45.584 -10.415  47.852  1.00 97.99      AAAA N
ATOM    373  CA  ASP    39      46.821 -11.148  47.980  1.00 99.19      AAAA C
ATOM    374  CB  ASP    39      47.579 -11.050  46.652  1.00102.13      AAAA C
ATOM    375  CG  ASP    39      47.696 -12.387  45.948  0.01101.22      AAAA C
ATOM    376  OD1 ASP    39      46.644 -12.978  45.623  0.01101.42      AAAA O
ATOM    377  OD2 ASP    39      48.833 -12.848  45.718  0.01101.41      AAAA O
ATOM    378  C   ASP    39      47.660 -10.564  49.105  1.00 99.40      AAAA C
ATOM    379  O   ASP    39      47.692 -11.056  50.224  1.00 99.15      AAAA O
ATOM    380  N   TYR    40      48.354  -9.479  48.818  1.00100.96      AAAA N
ATOM    382  CA  TYR    40      49.120  -8.706  49.802  1.00101.16      AAAA C
ATOM    383  CB  TYR    40      49.511  -7.393  49.130  1.00103.67      AAAA C
ATOM    384  CG  TYR    40      50.159  -6.281  49.887  1.00107.81      AAAA C
ATOM    385  CD1 TYR    40      50.931  -5.325  49.228  1.00109.56      AAAA C
ATOM    386  CE1 TYR    40      51.540  -4.280  49.910  1.00109.67      AAAA C
ATOM    387  CD2 TYR    40      50.044  -6.115  51.254  1.00109.28      AAAA C
ATOM    388  CE2 TYR    40      50.618  -5.102  51.976  1.00109.83      AAAA C
ATOM    389  CZ  TYR    40      51.372  -4.181  51.276  1.00110.16      AAAA C
ATOM    390  OH  TYR    40      51.999  -3.127  51.893  1.00109.84      AAAA O
ATOM    392  C   TYR    40      48.343  -8.529  51.100  1.00 99.10      AAAA C
ATOM    393  O   TYR    40      47.168  -8.182  51.183  1.00 99.05      AAAA O
ATOM    394  N   LYS    41      49.041  -8.653  52.218  1.00 98.62      AAAA N
ATOM    396  CA  LYS    41      48.443  -8.549  53.546  1.00100.30      AAAA C
ATOM    397  CB  LYS    41      49.385  -9.160  54.599  1.00104.42      AAAA C
ATOM    398  CG  LYS    41      49.218 -10.649  54.814  0.01101.06      AAAA C
ATOM    399  CD  LYS    41      47.776 -11.107  54.919  0.01100.66      AAAA C
ATOM    400  CE  LYS    41      47.205 -10.880  56.308  0.01 99.86      AAAA C
ATOM    401  NZ  LYS    41      47.882 -11.728  57.328  0.01 99.62      AAAA N
ATOM    405  C   LYS    41      48.035  -7.136  53.947  1.00 98.99      AAAA C
ATOM    406  O   LYS    41      47.615  -6.371  53.057  1.00103.33      AAAA O
ATOM    407  N   SER    42      48.198  -6.754  55.221  1.00 91.75      AAAA N
ATOM    409  CA  SER    42      47.825  -5.412  55.604  1.00 85.06      AAAA C
ATOM    410  CB  SER    42      46.385  -5.520  56.147  1.00 95.33      AAAA C
ATOM    411  OG  SER    42      46.547  -6.140  57.426  1.00104.63      AAAA O
ATOM    413  C   SER    42      48.628  -4.715  56.687  1.00 80.78      AAAA C
ATOM    414  O   SER    42      49.326  -5.259  57.538  1.00 81.03      AAAA O
ATOM    415  N   TYR    43      48.495  -3.395  56.676  1.00 73.03      AAAA N
ATOM    417  CA  TYR    43      49.069  -2.488  57.635  1.00 67.25      AAAA C
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ATOM    418  CB  TYR    43      49.086  -1.119  56.965  1.00 65.37      AAAA C
ATOM    419  CG  TYR    43      49.953  -1.021  55.727  1.00 63.92      AAAA C
ATOM    420  CD1 TYR    43      50.931  -1.935  55.406  1.00 63.87      AAAA C
ATOM    421  CE1 TYR    43      51.698  -1.781  54.274  1.00 66.09      AAAA C
ATOM    422  CD2 TYR    43      49.770   0.050  54.870  1.00 63.30      AAAA C
ATOM    423  CE2 TYR    43      50.536   0.214  53.728  1.00 67.62      AAAA C
ATOM    424  CZ  TYR    43      51.508  -0.712  53.432  1.00 66.94      AAAA C
ATOM    425  OH  TYR    43      52.262  -0.563  52.305  1.00 65.23      AAAA O
ATOM    427  C   TYR    43      48.248  -2.381  58.925  1.00 64.88      AAAA C
ATOM    428  O   TYR    43      47.088  -2.851  59.030  1.00 62.90      AAAA O
ATOM    429  N   ARG    44      48.782  -1.567  59.825  1.00 57.88      AAAA N
ATOM    431  CA  ARG    44      48.019  -1.285  61.039  1.00 56.45      AAAA C
ATOM    432  CB  ARG    44      47.842  -2.611  61.760  1.00 46.51      AAAA C
ATOM    433  CG  ARG    44      47.815  -2.375  63.244  1.00 54.66      AAAA C
ATOM    434  CD  ARG    44      46.885  -3.327  63.986  1.00 58.54      AAAA C
ATOM    435  NE  ARG    44      47.090  -2.927  65.403  1.00 68.56      AAAA N
ATOM    437  CZ  ARG    44      46.464  -3.536  66.395  1.00 64.82      AAAA C
ATOM    438  NH1 ARG    44      45.644  -4.529  66.132  1.00 61.63      AAAA N
ATOM    441  NH2 ARG    44      46.674  -3.139  67.628  1.00 66.03      AAAA N
ATOM    444  C   ARG    44      48.811  -0.285  61.845  1.00 55.59      AAAA C
ATOM    445  O   ARG    44      49.916  -0.552  62.320  1.00 58.43      AAAA O
ATOM    446  N   PHE    45      48.276   0.866  62.139  1.00 51.13      AAAA N
ATOM    448  CA  PHE    45      48.865   1.944  62.863  1.00 45.94      AAAA C
ATOM    449  CB  PHE    45      48.774   3.249  61.978  1.00 35.89      AAAA C
ATOM    450  CG  PHE    45      49.106   2.937  60.554  1.00 30.29      AAAA C
ATOM    451  CD1 PHE    45      50.373   3.051  59.998  1.00 45.72      AAAA C
ATOM    452  CD2 PHE    45      48.127   2.428  59.728  1.00 35.95      AAAA C
ATOM    453  CE1 PHE    45      50.653   2.715  58.672  1.00 47.76      AAAA C
ATOM    454  CE2 PHE    45      48.358   2.096  58.406  1.00 39.92      AAAA C
ATOM    455  CZ  PHE    45      49.612   2.244  57.967  1.00 46.44      AAAA C
ATOM    456  C   PHE    45      48.181   2.123  64.203  1.00 41.65      AAAA C
ATOM    457  O   PHE    45      47.708   3.223  64.475  1.00 40.99      AAAA O
ATOM    458  N   PRO    46      48.494   1.338  65.212  1.00 43.20      AAAA N
ATOM    459  CD  PRO    46      49.300   0.097  65.132  1.00 47.74      AAAA C
ATOM    460  CA  PRO    46      48.032   1.530  66.560  1.00 43.34      AAAA C
ATOM    461  CB  PRO    46      48.514   0.319  67.380  1.00 44.92      AAAA C
ATOM    462  CG  PRO    46      49.404  -0.464  66.514  1.00 45.48      AAAA C
ATOM    463  C   PRO    46      48.558   2.768  67.233  1.00 41.30      AAAA C
ATOM    464  O   PRO    46      48.329   2.830  68.443  1.00 44.57      AAAA O
ATOM    465  N   LYS    47      49.450   3.533  66.676  1.00 39.33      AAAA N
ATOM    467  CA  LYS    47      49.991   4.679  67.362  1.00 38.10      AAAA C
ATOM    468  CB  LYS    47      51.378   4.981  66.852  1.00 48.07      AAAA C
ATOM    469  CG  LYS    47      52.032   3.995  65.902  1.00 67.95      AAAA C
ATOM    470  CD  LYS    47      53.563   3.976  65.891  1.00 61.33      AAAA C
ATOM    471  CE  LYS    47      54.115   4.648  67.147  1.00 72.19      AAAA C
ATOM    472  NZ  LYS    47      54.024   6.132  66.874  1.00 79.29      AAAA N
ATOM    476  C   LYS    47      49.014   5.848  67.195  1.00 39.76      AAAA C
ATOM    477  O   LYS    47      49.189   6.827  67.952  1.00 35.45      AAAA O
ATOM    478  N   LEU    48      48.300   5.886  66.053  1.00 36.45      AAAA N
ATOM    480  CA  LEU    48      47.370   7.004  65.800  1.00 40.40      AAAA C
ATOM    481  CB  LEU    48      46.823   6.919  64.389  1.00 28.59      AAAA C
ATOM    482  CG  LEU    48      45.947   7.967  63.787  1.00 31.04      AAAA C
ATOM    483  CD1 LEU    48      46.637   9.310  63.878  1.00 36.86      AAAA C
ATOM    484  CD2 LEU    48      45.591   7.738  62.294  1.00 34.49      AAAA C
ATOM    485  C   LEU    48      46.186   7.022  66.807  1.00 42.21      AAAA C
ATOM    486  O   LEU    48      45.271   6.187  66.863  1.00 36.48      AAAA O
ATOM    487  N   THR    49      46.138   8.041  67.673  1.00 38.95      AAAA N
ATOM    489  CA  THR    49      45.045   8.151  68.574  1.00 37.96      AAAA C
ATOM    490  CB  THR    49      45.548   8.207  70.034  1.00 48.69      AAAA C
ATOM    491  OG1 THR    49      46.396   9.340  70.225  1.00 35.90      AAAA O
ATOM    493  CG2 THR    49      46.230   6.957  70.529  1.00 31.99      AAAA C
ATOM    494  C   THR    49      44.230   9.425  68.321  1.00 39.48      AAAA C
ATOM    495  O   THR    49      43.111   9.451  68.837  1.00 34.49      AAAA O
ATOM    496  N   VAL    50      44.735  10.415  67.605  1.00 37.32      AAAA N
ATOM    498  CA  VAL    50      43.995  11.664  67.418  1.00 38.72      AAAA C
ATOM    499  CB  VAL    50      44.293  12.708  68.503  1.00 37.24      AAAA C
ATOM    500  CG1 VAL    50      43.630  14.066  68.208  1.00 29.96      AAAA C
ATOM    501  CG2 VAL    50      43.884  12.311  69.913  1.00 32.52      AAAA C
ATOM    502  C   VAL    50      44.271  12.305  66.048  1.00 37.03      AAAA C
ATOM    503  O   VAL    50      45.195  11.863  65.431  1.00 37.96      AAAA O
ATOM    504  N   ILE    51      43.319  12.939  65.415  1.00 37.49      AAAA N
ATOM    506  CA  ILE    51      43.301  13.575  64.133  1.00 32.48      AAAA C
ATOM    507  CB  ILE    51      42.346  12.864  63.152  1.00 34.51      AAAA C
ATOM    508  CG2 ILE    51      41.995  13.802  61.978  1.00 32.31      AAAA C
ATOM    509  CG1 ILE    51      43.026  11.611  62.671  1.00 30.78      AAAA C
ATOM    510  CD1 ILE    51      42.358  10.559  61.815  1.00 19.69      AAAA C
ATOM    511  C   ILE    51      42.659  14.939  64.431  1.00 34.14      AAAA C
ATOM    512  O   ILE    51      41.546  14.830  64.923  1.00 29.08      AAAA O
ATOM    513  N   THR    52      43.342  16.058  64.238  1.00 33.93      AAAA N
ATOM    515  CA  THR    52      42.806  17.305  64.719  1.00 33.83      AAAA C
ATOM    516  CB  THR    52      43.961  18.338  64.939  1.00 35.39      AAAA C
ATOM    517  OG1 THR    52      44.726  18.567  63.781  1.00 41.28      AAAA O
ATOM    519  CG2 THR    52      44.775  17.926  66.134  1.00 22.01      AAAA C
ATOM    520  C   THR    52      41.741  17.961  63.863  1.00 39.02      AAAA C
ATOM    521  O   THR    52      41.202  19.030  64.243  1.00 38.88      AAAA O
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ATOM    522  H   GLU    53      41.524  17.477  62.639  1.00 36.93      AAAA H
ATOM    524  CA  GLU    53      40.434  17.953  61.785  1.00 38.38      AAAA C
ATOM    525  CB  GLU    53      41.064  18.512  60.483  1.00 29.76      AAAA C
ATOM    526  CG  GLU    53      42.061  19.552  60.834  1.00 30.48      AAAA C
ATOM    527  CD  GLU    53      42.517  20.396  59.697  1.00 40.82      AAAA C
ATOM    528  OE1 GLU    53      42.638  19.908  58.556  1.00 57.56      AAAA O
ATOM    529  OE2 GLU    53      42.799  21.559  59.931  1.00 35.74      AAAA O
ATOM    530  C   GLU    53      39.506  16.789  61.388  1.00 39.19      AAAA C
ATOM    531  O   GLU    53      38.922  16.311  62.386  1.00 38.95      AAAA O
ATOM    532  H   TYR    54      39.639  16.353  60.102  1.00 30.60      AAAA H
ATOM    534  CA  TYR    54      38.666  15.342  59.713  1.00 35.96      AAAA C
ATOM    535  CB  TYR    54      37.654  15.802  58.636  1.00 30.71      AAAA C
ATOM    536  CG  TYR    54      38.247  16.476  57.388  1.00 21.18      AAAA C
ATOM    537  CD1 TYR    54      38.487  15.733  56.305  1.00 20.22      AAAA C
ATOM    538  CE1 TYR    54      38.980  16.243  55.086  1.00 21.04      AAAA C
ATOM    539  CD2 TYR    54      38.577  17.844  57.307  1.00 23.97      AAAA C
ATOM    540  CE2 TYR    54      39.049  18.384  56.124  1.00 24.69      AAAA C
ATOM    541  CZ  TYR    54      39.263  17.569  55.032  1.00 26.72      AAAA C
ATOM    542  OH  TYR    54      39.763  18.047  53.847  1.00 37.55      AAAA O
ATOM    544  C   TYR    54      39.405  14.115  59.142  1.00 33.87      AAAA C
ATOM    545  O   TYR    54      40.513  14.360  58.678  1.00 30.40      AAAA O
ATOM    546  H   LEU    55      38.683  13.021  59.004  1.00 23.24      AAAA H
ATOM    548  CA  LEU    55      39.111  11.812  58.454  1.00 30.08      AAAA C
ATOM    549  CB  LEU    55      39.011  10.663  59.510  1.00 14.78      AAAA C
ATOM    550  CG  LEU    55      39.349   9.314  58.818  1.00 26.98      AAAA C
ATOM    551  CD1 LEU    55      40.668   9.477  58.040  1.00 26.66      AAAA C
ATOM    552  CD2 LEU    55      39.496   8.093  59.705  1.00 14.45      AAAA C
ATOM    553  C   LEU    55      38.201  11.548  57.238  1.00 37.43      AAAA C
ATOM    554  O   LEU    55      36.995  11.632  57.427  1.00 39.55      AAAA O
ATOM    555  H   LEU    56      38.700  11.348  56.035  1.00 41.83      AAAA H
ATOM    557  CA  LEU    56      37.955  11.201  54.799  1.00 36.98      AAAA C
ATOM    558  CB  LEU    56      37.998  12.446  53.949  1.00 33.29      AAAA C
ATOM    559  CG  LEU    56      37.984  12.514  52.416  1.00 30.35      AAAA C
ATOM    560  CD1 LEU    56      37.076  11.460  51.821  1.00 47.95      AAAA C
ATOM    561  CD2 LEU    56      37.286  13.807  51.985  1.00 33.47      AAAA C
ATOM    562  C   LEU    56      38.595  10.047  54.008  1.00 39.75      AAAA C
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ATOM    564  H   LEU    57      37.846   9.008  53.800  1.00 36.68      AAAA H
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ATOM    568  CG  LEU    57      39.064   6.534  55.026  1.00 36.13      AAAA C
ATOM    569  CD1 LEU    57      38.513   6.890  56.417  1.00 33.26      AAAA C
ATOM    570  CD2 LEU    57      39.630   5.162  55.039  1.00 24.11      AAAA C
ATOM    571  C   LEU    57      37.203   7.825  51.838  1.00 46.03      AAAA C
ATOM    572  O   LEU    57      35.985   7.993  51.969  1.00 44.78      AAAA O
ATOM    573  H   PHE    58      37.792   7.898  50.642  1.00 47.07      AAAA H
ATOM    575  CA  PHE    58      36.895   8.002  49.467  1.00 48.75      AAAA C
ATOM    576  CB  PHE    58      36.704   9.448  49.102  1.00 46.67      AAAA C
ATOM    577  CG  PHE    58      36.447   9.815  47.692  1.00 54.66      AAAA C
ATOM    578  CD1 PHE    58      37.413   9.706  46.697  1.00 55.19      AAAA C
ATOM    579  CD2 PHE    58      35.200  10.301  47.326  1.00 53.86      AAAA C
ATOM    580  CE1 PHE    58      37.124  10.063  45.396  1.00 50.36      AAAA C
ATOM    581  CE2 PHE    58      34.885  10.655  46.011  1.00 41.84      AAAA C
ATOM    582  CZ  PHE    58      35.877  10.521  45.037  1.00 46.50      AAAA C
ATOM    583  C   PHE    58      37.351   7.052  48.379  1.00 49.71      AAAA C
ATOM    584  O   PHE    58      38.487   7.073  47.934  1.00 52.16      AAAA O
ATOM    585  H   ARG    59      36.471   6.118  47.944  1.00 44.26      AAAA H
ATOM    587  CA  ARG    59      36.753   5.281  46.815  1.00 40.80      AAAA C
ATOM    588  CB  ARG    59      36.911   5.993  45.427  1.00 23.79      AAAA C
ATOM    589  CG  ARG    59      35.869   7.020  45.121  1.00 46.53      AAAA C
ATOM    590  CD  ARG    59      35.921   7.562  43.706  1.00 37.64      AAAA C
ATOM    591  NE  ARG    59      35.822   6.422  42.806  1.00 49.23      AAAA H
ATOM    593  CZ  ARG    59      34.950   5.832  42.036  1.00 41.36      AAAA C
ATOM    594  NH1 ARG    59      33.702   6.277  41.931  1.00 47.00      AAAA H
ATOM    597  NH2 ARG    59      35.237   4.729  41.327  1.00 42.58      AAAA H
ATOM    600  C   ARG    59      38.037   4.494  47.049  1.00 42.25      AAAA C
ATOM    601  O   ARG    59      38.981   4.513  46.232  1.00 44.11      AAAA O
ATOM    602  H   VAL    60      38.001   3.625  48.023  1.00 40.84      AAAA H
ATOM    604  CA  VAL    60      39.101   2.743  48.341  1.00 39.14      AAAA C
ATOM    605  CB  VAL    60      39.624   3.066  49.751  1.00 40.12      AAAA C
ATOM    606  CG1 VAL    60      40.407   1.872  50.296  1.00 35.05      AAAA C
ATOM    607  CG2 VAL    60      40.425   4.352  49.893  1.00 28.86      AAAA C
ATOM    608  C   VAL    60      38.539   1.337  48.368  1.00 43.56      AAAA C
ATOM    609  O   VAL    60      37.535   1.224  49.072  1.00 47.66      AAAA O
ATOM    610  N   ALA    61      39.094   0.371  47.659  1.00 41.92      AAAA H
ATOM    612  CA  ALA    61      38.617  -0.992  47.749  1.00 42.05      AAAA C
ATOM    613  CB  ALA    61      38.302  -1.483  46.364  1.00 52.40      AAAA C
ATOM    614  C   ALA    61      39.613  -1.934  48.386  1.00 43.08      AAAA C
ATOM    615  O   ALA    61      40.757  -1.602  48.670  1.00 50.59      AAAA O
ATOM    616  N   GLY    62      39.200  -3.105  48.849  1.00 45.71      AAAA N
ATOM    618  CA  GLY    62      40.136  -4.079  49.385  1.00 45.39      AAAA C
ATOM    619  C   GLY    62      40.262  -3.902  50.872  1.00 48.04      AAAA C
ATOM    620  O   GLY    62      40.587  -4.835  51.604  1.00 52.34      AAAA O
ATOM    621  H   LEU    63      39.985  -2.734  51.385  1.00 46.90      AAAA H
ATOM    623  CA  LEU    63      40.003  -2.443  52.805  1.00 49.11      AAAA C
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ATOM    624  CB  LEU    63      40.274  -0.953  53.027  1.00 41.41      AAAA C
ATOM    625  CG  LEU    63      40.265  -0.423  54.443  1.00 53.41      AAAA C
ATOM    626  CD1 LEU    63      41.172  -1.164  55.416  1.00 48.27      AAAA C
ATOM    627  CD2 LEU    63      40.637   1.047  54.246  1.00 50.51      AAAA C
ATOM    628  C   LEU    63      38.643  -2.881  53.323  1.00 54.20      AAAA C
ATOM    629  O   LEU    63      37.587  -2.430  52.837  1.00 57.73      AAAA O
ATOM    630  N   GLU    64      38.658  -3.862  54.190  1.00 53.97      AAAA N
ATOM    632  CA  GLU    64      37.462  -4.448  54.749  1.00 56.96      AAAA C
ATOM    633  CB  GLU    64      37.689  -5.956  54.734  1.00 65.33      AAAA C
ATOM    634  CG  GLU    64      37.832  -6.484  53.293  1.00 75.14      AAAA C
ATOM    635  CD  GLU    64      37.404  -7.940  53.128  1.00 78.10      AAAA C
ATOM    636  OE1 GLU    64      37.424  -8.698  54.132  1.00 63.93      AAAA O
ATOM    637  OE2 GLU    64      37.036  -8.320  51.978  1.00 88.77      AAAA O
ATOM    638  C   GLU    64      37.096  -4.007  56.163  1.00 57.12      AAAA C
ATOM    639  O   GLU    64      35.986  -4.332  56.600  1.00 59.82      AAAA O
ATOM    640  N   SER    65      37.766  -3.042  56.761  1.00 50.64      AAAA N
ATOM    642  CA  SER    65      37.539  -2.523  58.060  1.00 47.19      AAAA C
ATOM    643  CB  SER    65      37.743  -3.596  59.139  1.00 49.24      AAAA C
ATOM    644  OG  SER    65      37.501  -2.971  60.429  1.00 50.90      AAAA O
ATOM    646  C   SER    65      38.516  -1.405  58.432  1.00 48.35      AAAA C
ATOM    647  O   SER    65      39.716  -1.692  58.374  1.00 52.75      AAAA O
ATOM    648  N   LEU    66      38.054  -0.289  58.984  1.00 41.03      AAAA N
ATOM    650  CA  LEU    66      38.956   0.758  59.405  1.00 41.94      AAAA C
ATOM    651  CB  LEU    66      38.247   2.083  59.498  1.00 25.25      AAAA C
ATOM    652  CG  LEU    66      37.283   2.476  58.402  1.00 34.49      AAAA C
ATOM    653  CD1 LEU    66      36.974   3.951  58.512  1.00 30.81      AAAA C
ATOM    654  CD2 LEU    66      37.767   2.200  56.994  1.00 34.34      AAAA C
ATOM    655  C   LEU    66      39.646   0.462  60.734  1.00 45.39      AAAA C
ATOM    656  O   LEU    66      40.762   0.947  60.927  1.00 41.05      AAAA O
ATOM    657  N   GLY    67      39.000  -0.346  61.583  1.00 45.21      AAAA N
ATOM    659  CA  GLY    67      39.773  -0.672  62.799  1.00 48.14      AAAA C
ATOM    660  C   GLY    67      40.998  -1.508  62.445  1.00 44.51      AAAA C
ATOM    661  O   GLY    67      41.855  -1.724  63.287  1.00 45.42      AAAA O
ATOM    662  N   ASP    68      41.013  -2.189  61.309  1.00 47.60      AAAA N
ATOM    664  CA  ASP    68      42.194  -2.834  60.738  1.00 50.99      AAAA C
ATOM    665  CB  ASP    68      42.012  -3.417  59.361  1.00 39.43      AAAA C
ATOM    666  CG  ASP    68      41.205  -4.678  59.311  1.00 45.82      AAAA C
ATOM    667  OD1 ASP    68      40.912  -5.341  60.320  1.00 44.69      AAAA O
ATOM    668  OD2 ASP    68      40.819  -5.065  58.187  1.00 47.23      AAAA O
ATOM    669  C   ASP    68      43.363  -1.837  60.596  1.00 45.89      AAAA C
ATOM    670  O   ASP    68      44.436  -2.269  60.903  1.00 44.84      AAAA O
ATOM    671  N   LEU    69      43.145  -0.609  60.247  1.00 42.49      AAAA N
ATOM    673  CA  LEU    69      44.175   0.352  60.048  1.00 45.80      AAAA C
ATOM    674  CB  LEU    69      43.920   1.393  58.945  1.00 45.25      AAAA C
ATOM    675  CG  LEU    69      43.902   0.882  57.494  1.00 54.25      AAAA C
ATOM    676  CD1 LEU    69      43.541   2.037  56.565  1.00 47.26      AAAA C
ATOM    677  CD2 LEU    69      45.211   0.200  57.113  1.00 50.76      AAAA C
ATOM    678  C   LEU    69      44.347   1.107  61.350  1.00 49.50      AAAA C
ATOM    679  O   LEU    69      45.470   1.210  61.851  1.00 54.51      AAAA O
ATOM    680  N   PHE    70      43.296   1.737  61.869  1.00 44.60      AAAA N
ATOM    682  CA  PHE    70      43.423   2.564  63.046  1.00 39.67      AAAA C
ATOM    683  CB  PHE    70      42.987   3.973  62.700  1.00 26.08      AAAA C
ATOM    684  CG  PHE    70      43.465   4.501  61.390  1.00 45.32      AAAA C
ATOM    685  CD1 PHE    70      42.532   4.748  60.384  1.00 47.41      AAAA C
ATOM    686  CD2 PHE    70      44.815   4.767  61.130  1.00 48.77      AAAA C
ATOM    687  CE1 PHE    70      42.945   5.263  59.159  1.00 56.16      AAAA C
ATOM    688  CE2 PHE    70      45.229   5.256  59.895  1.00 47.24      AAAA C
ATOM    689  CZ  PHE    70      44.293   5.506  58.896  1.00 49.54      AAAA C
ATOM    690  C   PHE    70      42.655   1.999  64.219  1.00 40.09      AAAA C
ATOM    691  O   PHE    70      41.874   2.734  64.838  1.00 35.74      AAAA O
ATOM    692  N   PRO    71      43.053   0.852  64.768  1.00 39.19      AAAA N
ATOM    693  CD  PRO    71      44.269   0.058  64.411  1.00 39.94      AAAA C
ATOM    694  CA  PRO    71      42.444   0.237  65.899  1.00 35.30      AAAA C
ATOM    695  CB  PRO    71      43.308  -0.983  66.246  1.00 38.03      AAAA C
ATOM    696  CG  PRO    71      44.669  -0.564  65.717  1.00 38.36      AAAA C
ATOM    697  C   PRO    71      42.453   1.089  67.126  1.00 33.72      AAAA C
ATOM    698  O   PRO    71      42.005   0.630  68.159  1.00 39.32      AAAA O
ATOM    699  N   ASN    72      43.058   2.220  67.231  1.00 36.55      AAAA N
ATOM    701  CA  ASN    72      43.204   3.032  68.401  1.00 32.60      AAAA C
ATOM    702  CB  ASN    72      44.637   2.916  68.962  1.00 36.89      AAAA C
ATOM    703  CG  ASN    72      44.735   1.638  69.761  1.00 47.03      AAAA C
ATOM    704  OD1 ASN    72      44.644   1.619  70.979  1.00 64.42      AAAA O
ATOM    705  ND2 ASN    72      44.880   0.475  69.169  1.00 63.17      AAAA N
ATOM    708  C   ASN    72      42.875   4.477  68.135  1.00 30.11      AAAA C
ATOM    709  O   ASN    72      43.099   5.201  69.104  1.00 36.53      AAAA O
ATOM    710  N   LEU    73      42.309   4.809  66.978  1.00 27.62      AAAA N
ATOM    712  CA  LEU    73      41.940   6.207  66.730  1.00 34.07      AAAA C
ATOM    713  CB  LEU    73      41.476   6.373  65.292  1.00 28.37      AAAA C
ATOM    714  CG  LEU    73      40.819   7.713  64.882  1.00 29.33      AAAA C
ATOM    715  CD1 LEU    73      41.918   8.721  64.963  1.00 31.86      AAAA C
ATOM    716  CD2 LEU    73      40.202   7.518  63.478  1.00 32.07      AAAA C
ATOM    717  C   LEU    73      40.929   6.569  67.817  1.00 32.14      AAAA C
ATOM    718  O   LEU    73      40.073   5.737  68.081  1.00 35.02      AAAA O
ATOM    719  N   THR    74      41.081   7.585  68.582  1.00 29.47      AAAA N
ATOM    721  CA  THR    74      40.150   7.826  69.683  1.00 34.80      AAAA C
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ATOM    722  CB  THR    74      41.028   7.744  70.952  1.00 46.09      AAAA C
ATOM    723  OG1 THR    74      41.729   6.485  70.880  1.00 46.30      AAAA O
ATOM    725  CG2 THR    74      40.262   7.831  72.253  1.00 39.45      AAAA C
ATOM    726  C   THR    74      39.424   9.155  69.602  1.00 35.48      AAAA C
ATOM    727  O   THR    74      38.270   9.322  70.077  1.00 35.32      AAAA O
ATOM    728  N   VAL    75      40.047  10.198  69.073  1.00 29.80      AAAA N
ATOM    730  CA  VAL    75      39.351  11.474  68.892  1.00 34.91      AAAA C
ATOM    731  CB  VAL    75      39.856  12.445  69.955  1.00 26.03      AAAA C
ATOM    732  CG1 VAL    75      39.173  13.801  69.934  1.00 24.51      AAAA C
ATOM    733  CG2 VAL    75      39.675  11.910  71.366  1.00 19.87      AAAA C
ATOM    734  C   VAL    75      39.613  12.045  67.494  1.00 37.57      AAAA C
ATOM    735  O   VAL    75      40.724  11.808  67.022  1.00 35.99      AAAA O
ATOM    736  N   ILE    76      38.600  12.555  66.796  1.00 35.91      AAAA N
ATOM    738  CA  ILE    76      38.696  13.340  65.592  1.00 31.48      AAAA C
ATOM    739  CB  ILE    76      37.831  12.769  64.492  1.00 29.60      AAAA C
ATOM    740  CG2 ILE    76      37.856  13.630  63.208  1.00 19.54      AAAA C
ATOM    741  CG1 ILE    76      38.222  11.314  64.277  1.00 28.52      AAAA C
ATOM    742  CD1 ILE    76      37.149  10.556  63.478  1.00 28.85      AAAA C
ATOM    743  C   ILE    76      38.157  14.718  66.000  1.00 33.84      AAAA C
ATOM    744  O   ILE    76      36.987  14.777  66.274  1.00 38.84      AAAA O
ATOM    745  N   ARG    77      38.906  15.733  66.230  1.00 30.32      AAAA N
ATOM    747  CA  ARG    77      38.605  16.901  67.021  1.00 30.82      AAAA C
ATOM    748  CB  ARG    77      39.961  17.475  67.461  1.00 26.62      AAAA C
ATOM    749  CG  ARG    77      39.993  18.836  68.058  1.00 52.42      AAAA C
ATOM    750  CD  ARG    77      41.290  18.957  68.908  1.00 49.10      AAAA C
ATOM    751  NE  ARG    77      41.411  17.817  69.773  1.00 39.23      AAAA N
ATOM    753  CZ  ARG    77      40.977  18.016  71.064  1.00 48.79      AAAA C
ATOM    754  NH1 ARG    77      40.440  19.104  71.610  1.00 30.34      AAAA N
ATOM    757  NH2 ARG    77      41.061  17.012  71.941  1.00 40.38      AAAA N
ATOM    760  C   ARG    77      37.643  17.733  66.225  1.00 31.75      AAAA C
ATOM    761  O   ARG    77      36.944  18.637  66.664  1.00 31.40      AAAA O
ATOM    762  N   GLY    78      37.688  17.661  64.884  1.00 32.87      AAAA N
ATOM    764  CA  GLY    78      36.982  18.409  63.950  1.00 16.23      AAAA C
ATOM    765  C   GLY    78      37.199  19.880  64.063  1.00 31.58      AAAA C
ATOM    766  O   GLY    78      36.363  20.775  63.674  1.00 34.03      AAAA O
ATOM    767  N   TRP    79      38.439  20.321  64.304  1.00 31.21      AAAA N
ATOM    769  CA  TRP    79      38.757  21.740  64.337  1.00 30.80      AAAA C
ATOM    770  CB  TRP    79      40.177  21.943  64.845  1.00 39.07      AAAA C
ATOM    771  CG  TRP    79      40.626  23.343  65.164  1.00 36.64      AAAA C
ATOM    772  CD2 TRP    79      41.691  24.001  64.433  1.00 28.52      AAAA C
ATOM    773  CE2 TRP    79      41.826  25.288  65.002  1.00 36.49      AAAA C
ATOM    774  CE3 TRP    79      42.473  23.625  63.370  1.00 37.96      AAAA C
ATOM    775  CD1 TRP    79      40.199  24.235  66.113  1.00 29.59      AAAA C
ATOM    776  NE1 TRP    79      40.917  25.413  66.054  1.00 27.67      AAAA N
ATOM    778  CZ2 TRP    79      42.770  26.213  64.543  1.00 31.83      AAAA C
ATOM    779  CZ3 TRP    79      43.389  24.548  62.876  1.00 46.14      AAAA C
ATOM    780  CH2 TRP    79      43.525  25.794  63.470  1.00 35.31      AAAA C
ATOM    781  C   TRP    79      38.606  22.418  62.986  1.00 28.75      AAAA C
ATOM    782  O   TRP    79      38.585  23.624  62.961  1.00 23.61      AAAA O
ATOM    783  N   LYS    80      38.659  21.684  61.895  1.00 31.84      AAAA N
ATOM    785  CA  LYS    80      38.305  22.153  60.573  1.00 32.78      AAAA C
ATOM    786  CB  LYS    80      39.453  22.498  59.689  1.00 41.17      AAAA C
ATOM    787  CG  LYS    80      39.838  23.911  59.470  1.00 34.68      AAAA C
ATOM    788  CD  LYS    80      41.025  24.350  60.306  1.00 44.77      AAAA C
ATOM    789  CE  LYS    80      41.276  25.811  59.898  1.00 50.41      AAAA C
ATOM    790  NZ  LYS    80      42.530  25.752  59.092  1.00 67.26      AAAA N
ATOM    791  C   LYS    80      37.585  20.960  59.917  1.00 34.52      AAAA C
ATOM    792  O   LYS    80      37.950  19.843  60.237  1.00 37.62      AAAA O
ATOM    793  N   LEU    81      36.477  21.267  59.207  1.00 31.77      AAAA N
ATOM    795  CA  LEU    81      35.742  20.157  58.600  1.00 31.02      AAAA C
ATOM    796  CB  LEU    81      34.290  20.315  59.092  1.00 31.20      AAAA C
ATOM    797  CG  LEU    81      34.115  20.319  60.632  1.00 36.97      AAAA C
ATOM    798  CD1 LEU    81      32.832  21.080  60.954  1.00 27.98      AAAA C
ATOM    799  CD2 LEU    81      34.089  18.955  61.297  1.00 28.77      AAAA C
ATOM    800  C   LEU    81      35.733  20.023  57.104  1.00 29.86      AAAA C
ATOM    801  O   LEU    81      36.082  20.947  56.368  1.00 29.34      AAAA O
ATOM    802  N   PHE    82      35.430  18.813  56.594  1.00 27.78      AAAA N
ATOM    804  CA  PHE    82      35.176  18.653  55.182  1.00 28.68      AAAA C
ATOM    805  CB  PHE    82      35.513  17.226  54.795  1.00 32.78      AAAA C
ATOM    806  CG  PHE    82      35.348  16.901  53.357  1.00 30.48      AAAA C
ATOM    807  CD1 PHE    82      36.378  17.130  52.447  1.00 32.86      AAAA C
ATOM    808  CD2 PHE    82      34.142  16.361  52.914  1.00 30.93      AAAA C
ATOM    809  CE1 PHE    82      36.217  16.769  51.104  1.00 43.27      AAAA C
ATOM    810  CE2 PHE    82      33.963  16.061  51.538  1.00 26.30      AAAA C
ATOM    811  CZ  PHE    82      35.005  16.238  50.672  1.00 37.73      AAAA C
ATOM    812  C   PHE    82      33.670  18.911  54.993  1.00 30.06      AAAA C
ATOM    813  O   PHE    82      32.830  18.045  55.278  1.00 27.36      AAAA O
ATOM    814  N   TYR    83      33.301  20.148  54.770  1.00 31.68      AAAA N
ATOM    815  CA  TYR    83      31.911  20.605  54.633  1.00 40.76      AAAA C
ATOM    816  C   TYR    83      31.043  19.977  55.726  1.00 44.00      AAAA C
ATOM    817  O   TYR    83      30.075  19.210  55.487  1.00 50.47      AAAA O
ATOM    818  CB  TYR    83      31.359  20.199  53.269  1.00 31.55      AAAA C
ATOM    819  CG  TYR    83      32.196  20.742  52.117  0.01 20.00      AAAA C
ATOM    820  CD1 TYR    83      33.254  19.982  51.609  0.01 20.00      AAAA C
ATOM    821  CD2 TYR    83      31.906  21.998  51.575  0.01 20.00      AAAA C
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ATOM    822  CE1 TYR    83      34.027  20.480  50.556  0.01 20.00      AAAA C
ATOM    823  CE2 TYR    83      32.679  22.496  50.521  0.01 20.00      AAAA C
ATOM    824  CZ  TYR    83      33.740  21.737  50.012  0.01 20.00      AAAA C
ATOM    825  OH  TYR    83      34.492  22.222  48.989  0.01 20.00      AAAA O
ATOM    826  N   ASN    84      31.043  20.461  56.924  1.00 40.91      AAAA N
ATOM    827  CA  ASN    84      30.250  20.057  58.056  1.00 36.54      AAAA C
ATOM    828  CB  ASN    84      28.763  20.046  57.700  1.00 47.84      AAAA C
ATOM    829  CG  ASN    84      28.274  21.164  56.797  1.00 60.75      AAAA C
ATOM    830  OD1 ASN    84      28.319  22.343  57.119  1.00 45.55      AAAA O
ATOM    831  ND2 ASN    84      27.839  20.876  55.552  1.00 65.98      AAAA N
ATOM    832  C   ASN    84      30.686  18.679  58.556  1.00 36.33      AAAA C
ATOM    833  O   ASN    84      30.137  18.206  59.580  1.00 38.24      AAAA O
ATOM    834  N   TYR    85      31.455  17.900  57.800  1.00 32.78      AAAA N
ATOM    836  CA  TYR    85      31.617  16.504  58.222  1.00 35.45      AAAA C
ATOM    837  CB  TYR    85      31.473  15.579  57.000  1.00 35.54      AAAA C
ATOM    838  CG  TYR    85      30.078  15.733  56.453  1.00 41.35      AAAA C
ATOM    839  CD1 TYR    85      29.868  16.291  55.199  1.00 38.22      AAAA C
ATOM    840  CE1 TYR    85      28.611  16.445  54.704  1.00 40.83      AAAA C
ATOM    841  CD2 TYR    85      28.954  15.371  57.200  1.00 47.42      AAAA C
ATOM    842  CE2 TYR    85      27.661  15.533  56.705  1.00 45.91      AAAA C
ATOM    843  CZ  TYR    85      27.497  16.072  55.445  1.00 46.06      AAAA C
ATOM    844  OH  TYR    85      26.258  16.315  54.886  1.00 46.05      AAAA O
ATOM    846  C   TYR    85      32.977  16.367  58.891  1.00 32.08      AAAA C
ATOM    847  O   TYR    85      33.943  16.977  58.495  1.00 37.44      AAAA O
ATOM    848  N   ALA    86      33.027  15.691  59.979  1.00 30.21      AAAA N
ATOM    850  CA  ALA    86      34.257  15.325  60.670  1.00 34.10      AAAA C
ATOM    851  CB  ALA    86      33.999  15.370  62.157  1.00 25.48      AAAA C
ATOM    852  C   ALA    86      34.729  13.962  60.216  1.00 32.67      AAAA C
ATOM    853  O   ALA    86      35.795  13.481  60.577  1.00 35.10      AAAA O
ATOM    854  N   LEU    87      33.832  13.173  59.597  1.00 28.56      AAAA N
ATOM    856  CA  LEU    87      34.188  11.805  59.323  1.00 29.26      AAAA C
ATOM    857  CB  LEU    87      33.798  10.860  60.471  1.00 13.64      AAAA C
ATOM    858  CG  LEU    87      33.801   9.363  60.188  1.00 25.77      AAAA C
ATOM    859  CD1 LEU    87      35.140   8.915  59.571  1.00 27.21      AAAA C
ATOM    860  CD2 LEU    87      33.637   8.432  61.393  1.00 23.52      AAAA C
ATOM    861  C   LEU    87      33.530  11.429  58.021  1.00 35.60      AAAA C
ATOM    862  O   LEU    87      32.320  11.421  58.001  1.00 38.97      AAAA O
ATOM    863  N   VAL    88      34.174  11.300  56.875  1.00 37.86      AAAA N
ATOM    865  CA  VAL    88      33.438  11.032  55.628  1.00 33.32      AAAA C
ATOM    866  CB  VAL    88      33.666  12.085  54.553  1.00 22.38      AAAA C
ATOM    867  CG1 VAL    88      32.974  11.675  53.261  1.00 19.24      AAAA C
ATOM    868  CG2 VAL    88      33.165  13.402  55.042  1.00 13.27      AAAA C
ATOM    869  C   VAL    88      33.898   9.684  55.114  1.00 31.79      AAAA C
ATOM    870  O   VAL    88      35.069   9.407  55.117  1.00 33.57      AAAA O
ATOM    871  N   ILE    89      33.078   8.728  54.822  1.00 31.08      AAAA N
ATOM    873  CA  ILE    89      33.361   7.433  54.280  1.00 30.45      AAAA C
ATOM    874  CB  ILE    89      32.941   6.384  55.296  1.00 30.17      AAAA C
ATOM    875  CG2 ILE    89      32.898   4.954  54.821  1.00 37.24      AAAA C
ATOM    876  CG1 ILE    89      33.893   6.420  56.500  1.00 24.92      AAAA C
ATOM    877  CD1 ILE    89      33.424   5.613  57.675  1.00 23.96      AAAA C
ATOM    878  C   ILE    89      32.509   7.206  53.027  1.00 40.64      AAAA C
ATOM    879  O   ILE    89      31.330   6.881  53.205  1.00 38.69      AAAA O
ATOM    880  N   PHE    90      33.082   7.464  51.845  1.00 41.45      AAAA N
ATOM    882  CA  PHE    90      32.346   7.371  50.591  1.00 37.67      AAAA C
ATOM    883  CB  PHE    90      32.347   8.776  50.110  1.00 32.17      AAAA C
ATOM    884  CG  PHE    90      31.581   9.081  48.865  1.00 39.77      AAAA C
ATOM    885  CD1 PHE    90      30.387   9.772  49.025  1.00 32.02      AAAA C
ATOM    886  CD2 PHE    90      32.052   8.721  47.620  1.00 29.28      AAAA C
ATOM    887  CE1 PHE    90      29.611  10.111  47.938  1.00 33.30      AAAA C
ATOM    888  CE2 PHE    90      31.290   9.086  46.534  1.00 43.09      AAAA C
ATOM    889  CZ  PHE    90      30.083   9.764  46.687  1.00 50.24      AAAA C
ATOM    890  C   PHE    90      32.856   6.384  49.557  1.00 40.72      AAAA C
ATOM    891  O   PHE    90      34.027   6.296  49.203  1.00 46.15      AAAA O
ATOM    892  N   GLU    91      32.024   5.519  49.001  1.00 39.16      AAAA N
ATOM    894  CA  GLU    91      32.248   4.601  47.954  1.00 42.45      AAAA C
ATOM    895  CB  GLU    91      32.479   5.231  46.583  1.00 38.08      AAAA C
ATOM    896  CG  GLU    91      31.136   5.865  46.250  1.00 58.86      AAAA C
ATOM    897  CD  GLU    91      30.855   5.776  44.757  1.00 63.55      AAAA C
ATOM    898  OE1 GLU    91      31.473   6.651  44.082  1.00 64.10      AAAA O
ATOM    899  OE2 GLU    91      30.058   4.813  44.573  1.00 63.64      AAAA O
ATOM    900  C   GLU    91      33.422   3.734  48.313  1.00 42.06      AAAA C
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ATOM    905  CB  MET    92      34.299   2.659  51.584  1.00 38.37      AAAA C
ATOM    906  CG  MET    92      35.412   2.156  52.420  1.00 59.39      AAAA C
ATOM    907  SD  MET    92      36.802   3.306  52.401  1.00 57.67      AAAA S
ATOM    908  CE  MET    92      36.340   4.405  51.108  1.00 38.36      AAAA C
ATOM    909  C   MET    92      34.012   1.005  49.745  1.00 43.37      AAAA C
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ATOM    913  CA  THR    93      34.175  -0.900  48.273  1.00 47.32      AAAA C
ATOM    914  CB  THR    93      34.666  -1.281  46.868  1.00 55.29      AAAA C
ATOM    915  OG1 THR    93      34.013  -0.488  45.892  1.00 57.81      AAAA O
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ATOM    923  CB  ASN    94      36.241  -4.315  50.001  1.00 59.01      AAAA C
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ATOM    957  CG  ASP    97      33.662  -3.562  60.624  1.00 56.95      AAAA C
ATOM    958  OD1 ASP    97      34.579  -2.825  61.012  1.00 59.88      AAAA O
ATOM    959  OD2 ASP    97      33.931  -4.782  60.714  1.00 56.01      AAAA O
ATOM    960  C   ASP    97      33.209  -1.224  59.201  1.00 41.25      AAAA C
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ATOM    973  CA  GLY    99      35.477  -0.972  63.121  1.00 33.74      AAAA C
ATOM    974  C   GLY    99      36.279  -0.084  64.024  1.00 35.90      AAAA C
ATOM    975  O   GLY    99      37.023  -0.572  64.899  1.00 38.21      AAAA O
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ATOM    981  CD1 LEU   100      36.710   5.479  62.610  1.00 21.38      AAAA C
ATOM    982  CD2 LEU   100      38.412   3.599  62.644  1.00 37.68      AAAA C
ATOM    983  C   LEU   100      36.312   1.976  66.194  1.00 31.94      AAAA C
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ATOM    990  CD1 TYR   101      38.571  -1.380  69.587  1.00 51.20      AAAA C
ATOM    991  CE1 TYR   101      39.901  -1.743  69.749  1.00 49.44      AAAA C
ATOM    992  CD2 TYR   101      38.615  -2.112  67.322  1.00 45.15      AAAA C
ATOM    993  CE2 TYR   101      39.927  -2.505  67.479  1.00 47.08      AAAA C
ATOM    994  CZ  TYR   101      40.548  -2.321  68.688  1.00 49.43      AAAA C
ATOM    995  OH  TYR   101      41.834  -2.662  68.997  1.00 55.82      AAAA O
ATOM    997  C   TYR   101      36.989   1.059  69.214  1.00 33.46      AAAA C
ATOM    998  O   TYR   101      36.630   0.813  70.375  1.00 43.00      AAAA O
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ATOM   1014  CG  LEU   103      35.525   7.482  66.612  1.00 30.32      AAAA C
ATOM   1015  CD1 LEU   103      36.606   8.513  66.646  1.00 23.29      AAAA C
ATOM   1016  CD2 LEU   103      35.199   7.169  65.146  1.00 37.19      AAAA C
ATOM   1017  C   LEU   103      35.484   6.508  69.691  1.00 37.31      AAAA C
ATOM   1018  O   LEU   103      34.449   5.874  69.837  1.00 34.24      AAAA O
ATOM   1019  N   ARG   104      35.810   7.456  70.563  1.00 33.31      AAAA N
ATOM   1021  CA  ARG   104      34.920   7.841  71.605  1.00 29.66      AAAA C
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ATOM	1023	CG	ARG	104	36.356	6.375	73.165	1.00	48.37	AAAA C
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ATOM	1025	NE	ARG	104	34.582	5.320	74.413	1.00	52.38	AAAA N
ATOM	1027	CZ	ARG	104	34.900	4.847	75.621	1.00	72.73	AAAA C
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ATOM   1134  OE2 GLU   114      25.787  10.106  48.488  1.00 35.53      AAAA O
ATOM   1135  C   GLU   114      28.039   6.072  50.944  1.00 44.17      AAAA C
ATOM   1136  O   GLU   114      29.120   5.538  51.090  1.00 49.97      AAAA O
ATOM   1137  N   LYS   115      27.191   5.556  50.096  1.00 40.55      AAAA N
ATOM   1139  CA  LYS   115      27.219   4.440  49.242  1.00 41.16      AAAA C
ATOM   1140  CB  LYS   115      27.275   4.764  47.718  1.00 23.62      AAAA C
ATOM   1141  CG  LYS   115      27.019   6.194  47.411  1.00 18.39      AAAA C
ATOM   1142  CD  LYS   115      26.537   6.355  45.982  1.00 24.74      AAAA C
ATOM   1143  CE  LYS   115      26.751   7.804  45.622  1.00 41.86      AAAA C
ATOM   1144  NZ  LYS   115      27.165   8.045  44.196  1.00 60.91      AAAA N
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ATOM   1153  CB  ASN   116      29.534   1.868  52.381  1.00 46.12      AAAA C
ATOM   1154  CG  ASN   116      30.372   3.153  52.345  1.00 48.92      AAAA C
ATOM   1155  OD1 ASN   116      31.337   3.016  51.583  1.00 38.59      AAAA O
ATOM   1156  ND2 ASN   116      29.927   4.174  53.056  1.00 37.35      AAAA N
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ATOM   1161  N   ALA   117      27.989  -0.188  49.772  1.00 40.94      AAAA N
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ATOM   1164  CB  ALA   117      27.494  -1.884  48.156  1.00 47.63      AAAA C
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ATOM   1166  O   ALA   117      26.211  -2.998  50.890  1.00 51.24      AAAA O
ATOM   1167  N   ASP   118      28.484  -2.823  51.005  1.00 47.43      AAAA N
ATOM   1169  CA  ASP   118      28.559  -3.980  51.920  1.00 45.74      AAAA C
ATOM   1170  CB  ASP   118      29.659  -4.945  51.477  1.00 55.39      AAAA C
ATOM   1171  CG  ASP   118      29.684  -5.119  49.958  1.00 59.40      AAAA C
ATOM   1172  OD1 ASP   118      28.870  -5.976  49.608  1.00 64.40      AAAA O
ATOM   1173  OD2 ASP   118      30.448  -4.447  49.207  1.00 66.73      AAAA O
ATOM   1174  C   ASP   118      28.818  -3.586  53.353  1.00 37.29      AAAA C
ATOM   1175  O   ASP   118      29.127  -4.536  54.026  1.00 42.89      AAAA O
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ATOM   1178  CA  LEU   119      28.986  -1.885  55.047  1.00 40.58      AAAA C
ATOM   1179  CB  LEU   119      29.159  -0.389  55.145  1.00 34.31      AAAA C
ATOM   1180  CG  LEU   119      29.640   0.331  56.378  1.00 36.58      AAAA C
ATOM   1181  CD1 LEU   119      30.950  -0.101  56.948  1.00 35.77      AAAA C
ATOM   1182  CD2 LEU   119      29.791   1.830  56.104  1.00 29.68      AAAA C
ATOM   1183  C   LEU   119      27.937  -2.376  56.007  1.00 43.67      AAAA C
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ATOM   1191  SG  CYS   120      26.568  -5.622  56.639  1.00 58.32      AAAA S
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ATOM   1195  CB  TYR   121      29.189  -3.572  62.130  1.00 34.61      AAAA C
ATOM   1196  CG  TYR   121      28.950  -5.032  62.519  1.00 36.52      AAAA C
ATOM   1197  CD1 TYR   121      29.087  -6.045  61.582  1.00 33.58      AAAA C
ATOM   1198  CE1 TYR   121      28.852  -7.350  61.980  1.00 41.21      AAAA C
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ATOM   1200  CE2 TYR   121      28.287  -6.630  64.201  1.00 39.48      AAAA C
ATOM   1201  CZ  TYR   121      28.432  -7.641  63.270  1.00 46.07      AAAA C
ATOM   1202  OH  TYR   121      28.161  -8.924  63.730  1.00 49.20      AAAA O
ATOM   1204  C   TYR   121      27.674  -1.523  61.789  1.00 38.83      AAAA C
ATOM   1205  O   TYR   121      28.445  -0.778  62.369  1.00 43.22      AAAA O
ATOM   1206  N   LEU   122      26.587  -1.045  61.180  1.00 39.58      AAAA N
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ATOM   1210  CG  LEU   122      26.497   2.014  59.108  1.00 44.44      AAAA C
ATOM   1211  CD1 LEU   122      25.778   2.448  57.859  1.00 32.19      AAAA C
ATOM   1212  CD2 LEU   122      26.136   3.057  60.170  1.00 47.76      AAAA C
ATOM   1213  C   LEU   122      25.212   0.910  61.935  1.00 44.85      AAAA C
ATOM   1214  O   LEU   122      25.269   1.759  62.839  1.00 47.66      AAAA O
ATOM   1215  N   SER   123      24.104   0.137  61.843  1.00 40.12      AAAA N
ATOM   1217  CA  SER   123      22.949   0.435  62.703  1.00 33.98      AAAA C
ATOM   1218  CB  SER   123      21.754  -0.330  62.239  1.00 19.26      AAAA C
ATOM   1219  OG  SER   123      21.964  -1.762  62.402  1.00 34.35      AAAA O
ATOM   1221  C   SER   123      23.165   0.060  64.159  1.00 37.43      AAAA C
ATOM   1222  O   SER   123      22.326   0.280  65.025  1.00 35.33      AAAA O
ATOM   1223  N   THR   124      24.242  -0.698  64.432  1.00 39.03      AAAA N
ATOM   1225  CA  THR   124      24.554  -1.165  65.753  1.00 37.79      AAAA C
ATOM   1226  CB  THR   124      25.368  -2.461  65.719  1.00 42.39      AAAA C
ATOM   1227  OG1 THR   124      26.502  -2.020  64.924  1.00 47.70      AAAA O
ATOM   1229  CG2 THR   124      24.677  -3.622  65.006  1.00 40.93      AAAA C
ATOM   1230  C   THR   124      25.522  -0.206  66.445  1.00 39.29      AAAA C
ATOM   1231  O   THR   124      25.948  -0.642  67.499  1.00 41.41      AAAA O
ATOM   1232  N   VAL   125      25.737   1.001  65.985  1.00 37.80      AAAA N
ATOM   1234  CA  VAL   125      26.594   1.964  66.661  1.00 41.06      AAAA C
ATOM   1235  CB  VAL   125      27.683   2.542  65.714  1.00 39.50      AAAA C
ATOM   1236  CG1 VAL   125      28.570   3.599  66.352  1.00 28.36      AAAA C
ATOM   1237  CG2 VAL   125      28.693   1.565  65.110  1.00 33.07      AAAA C
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ATOM   1238  C   VAL   125      25.759   3.127  67.179  1.00 41.17      AAAA C
ATOM   1239  O   VAL   125      24.941   3.750  66.531  1.00 41.22      AAAA O
ATOM   1240  N   ASP   126      26.072   3.636  68.367  1.00 44.54      AAAA N
ATOM   1242  CA  ASP   126      25.310   4.734  68.967  1.00 37.44      AAAA C
ATOM   1243  CB  ASP   126      24.862   4.335  70.342  1.00 34.73      AAAA C
ATOM   1244  CG  ASP   126      23.879   5.303  70.983  1.00 45.53      AAAA C
ATOM   1245  OD1 ASP   126      23.699   6.520  70.685  1.00 27.71      AAAA O
ATOM   1246  OD2 ASP   126      23.220   4.865  71.964  1.00 52.32      AAAA O
ATOM   1247  C   ASP   126      26.146   5.985  68.872  1.00 40.83      AAAA C
ATOM   1248  O   ASP   126      26.740   6.400  69.888  1.00 42.78      AAAA O
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ATOM   1252  CB  TRP   127      26.568   8.296  65.930  1.00 24.89      AAAA C
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ATOM   1254  CD2 TRP   127      28.587   7.208  64.518  1.00 28.60      AAAA C
ATOM   1255  CE2 TRP   127      28.631   6.186  63.579  1.00 29.06      AAAA C
ATOM   1256  CE3 TRP   127      29.778   7.845  64.873  1.00 35.51      AAAA C
ATOM   1257  CD1 TRP   127      26.465   6.450  64.188  1.00 18.67      AAAA C
ATOM   1258  NE1 TRP   127      27.311   5.712  63.394  1.00 42.87      AAAA N
ATOM   1260  CZ2 TRP   127      29.792   5.783  62.954  1.00 32.53      AAAA C
ATOM   1261  CZ3 TRP   127      30.972   7.445  64.285  1.00 31.51      AAAA C
ATOM   1262  CH2 TRP   127      30.937   6.405  63.336  1.00 37.86      AAAA C
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ATOM   1268  CB  SER   128      23.757  10.042  70.603  1.00 36.87      AAAA C
ATOM   1269  OG  SER   128      23.433   8.917  71.424  1.00 28.96      AAAA O
ATOM   1271  C   SER   128      26.133   9.975  71.292  1.00 32.39      AAAA C
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ATOM   1278  CD1 LEU   129      27.292   5.024  73.975  1.00 32.54      AAAA C
ATOM   1279  CD2 LEU   129      26.237   7.117  74.560  1.00 32.12      AAAA C
ATOM   1280  C   LEU   129      29.054   9.226  72.113  1.00 38.04      AAAA C
ATOM   1281  O   LEU   129      29.645  10.001  72.874  1.00 34.50      AAAA O
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ATOM   1285  CB  ILE   130      30.793   8.886  68.901  1.00 41.73      AAAA C
ATOM   1286  CG2 ILE   130      31.992   9.434  68.176  1.00 31.95      AAAA C
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ATOM   1288  CD1 ILE   130      31.053   6.457  68.165  1.00 42.65      AAAA C
ATOM   1289  C   ILE   130      30.305  11.178  69.679  1.00 46.48      AAAA C
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ATOM   1294  CB  LEU   131      28.499  12.616  67.259  1.00 46.81      AAAA C
ATOM   1295  CG  LEU   131      28.823  12.805  65.878  1.00 36.79      AAAA C
ATOM   1296  CD1 LEU   131      29.128  11.405  65.324  1.00 30.15      AAAA C
ATOM   1297  CD2 LEU   131      27.625  13.581  65.334  1.00 19.92      AAAA C
ATOM   1298  C   LEU   131      27.661  13.525  69.285  1.00 39.28      AAAA C
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ATOM   1300  N   ASP   132      27.742  14.811  69.518  1.00 33.73      AAAA N
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ATOM   1303  CB  ASP   132      27.017  16.944  70.381  1.00 43.17      AAAA C
ATOM   1304  CG  ASP   132      27.349  17.137  71.834  1.00 43.29      AAAA C
ATOM   1305  OD1 ASP   132      27.536  16.122  72.521  1.00 47.12      AAAA O
ATOM   1306  OD2 ASP   132      27.413  18.331  72.208  1.00 60.58      AAAA O
ATOM   1307  C   ASP   132      25.520  15.659  68.946  1.00 43.46      AAAA C
ATOM   1308  O   ASP   132      24.481  15.032  68.939  1.00 49.32      AAAA O
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ATOM   1312  CB  ALA   133      25.628  17.987  66.092  1.00 33.82      AAAA C
ATOM   1313  C   ALA   133      24.694  15.669  65.775  1.00 33.33      AAAA C
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ATOM   1317  CA  VAL   134      23.813  13.440  65.377  1.00 29.90      AAAA C
ATOM   1318  CB  VAL   134      23.202  12.241  66.120  1.00 40.63      AAAA C
ATOM   1319  CG1 VAL   134      24.265  11.441  66.855  1.00 35.20      AAAA C
ATOM   1320  CG2 VAL   134      22.095  12.701  67.068  1.00 30.84      AAAA C
ATOM   1321  C   VAL   134      22.735  13.732  64.353  1.00 36.98      AAAA C
ATOM   1322  O   VAL   134      22.616  13.106  63.292  1.00 32.95      AAAA O
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ATOM   1325  CA  SER   135      20.886  15.139  63.692  1.00 43.12      AAAA C
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ATOM   1337  HD2 ASN   136      24.379  19.441  62.585  1.00 47.85      AAAA H
ATOM   1340  C   ASN   136      24.031  15.230  60.259  1.00 35.31      AAAA C
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ATOM   1342  N   ASN   137      24.057  14.035  60.793  1.00 29.11      AAAA N
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ATOM   1345  CB  ASN   137      24.737  11.703  61.033  1.00 24.45      AAAA C
ATOM   1346  CG  ASN   137      25.631  11.965  62.217  1.00 26.63      AAAA C
ATOM   1347  OD1 ASN   137      26.070  13.121  62.369  1.00 30.22      AAAA O
ATOM   1348  ND2 ASN   137      25.830  10.923  63.000  1.00 18.90      AAAA N
ATOM   1351  C   ASN   137      23.950  12.749  58.817  1.00 35.89      AAAA C
ATOM   1352  O   ASN   137      22.716  12.755  58.855  1.00 38.57      AAAA O
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ATOM   1356  CB  TYR   138      24.682  12.861  55.421  1.00 27.10      AAAA C
ATOM   1357  CG  TYR   138      24.018  12.741  54.078  1.00 37.89      AAAA C
ATOM   1358  CD1 TYR   138      23.083  13.671  53.648  1.00 39.22      AAAA C
ATOM   1359  CE1 TYR   138      22.510  13.579  52.392  1.00 37.65      AAAA C
ATOM   1360  CD2 TYR   138      24.357  11.717  53.195  1.00 44.28      AAAA C
ATOM   1361  CE2 TYR   138      23.801  11.615  51.951  1.00 41.97      AAAA C
ATOM   1362  CZ  TYR   138      22.868  12.562  51.564  1.00 39.42      AAAA C
ATOM   1363  OH  TYR   138      22.296  12.504  50.318  1.00 45.48      AAAA O
ATOM   1365  C   TYR   138      24.373  10.578  56.051  1.00 31.33      AAAA C
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ATOM   1372  CG1 ILE   139      23.711   8.057  58.469  1.00 42.81      AAAA C
ATOM   1373  CD1 ILE   139      24.455   7.100  59.389  1.00 52.23      AAAA C
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ATOM   1376  N   VAL   140      23.286   6.997  53.873  1.00 35.29      AAAA N
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ATOM   1381  CG2 VAL   140      20.807   7.034  51.047  1.00 34.96      AAAA C
ATOM   1382  C   VAL   140      23.422   5.670  51.874  1.00 41.96      AAAA C
ATOM   1383  O   VAL   140      24.537   6.172  51.637  1.00 44.03      AAAA O
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ATOM   1386  CA  GLY   141      23.381   3.805  50.278  1.00 30.94      AAAA C
ATOM   1387  C   GLY   141      24.265   2.696  50.835  1.00 38.98      AAAA C
ATOM   1388  O   GLY   141      25.132   2.003  50.176  1.00 35.87      AAAA O
ATOM   1389  N   ASN   142      23.985   2.418  52.116  1.00 38.92      AAAA N
ATOM   1391  CA  ASN   142      24.858   1.390  52.746  1.00 44.32      AAAA C
ATOM   1392  CB  ASN   142      25.257   1.774  54.187  1.00 43.12      AAAA C
ATOM   1393  CG  ASN   142      26.131   3.022  54.152  1.00 42.00      AAAA C
ATOM   1394  OD1 ASN   142      26.984   3.077  53.269  1.00 40.47      AAAA O
ATOM   1395  ND2 ASN   142      25.945   4.022  55.019  1.00 41.98      AAAA N
ATOM   1398  C   ASN   142      24.153   0.066  52.687  1.00 45.84      AAAA C
ATOM   1399  O   ASN   142      23.113  -0.015  52.055  1.00 49.65      AAAA O
ATOM   1400  N   LYS   143      24.674  -0.990  53.272  1.00 45.23      AAAA N
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ATOM   1403  CB  LYS   143      25.166  -3.328  53.433  1.00 41.49      AAAA C
ATOM   1404  CG  LYS   143      24.750  -4.686  53.832  1.00 44.96      AAAA C
ATOM   1405  CD  LYS   143      25.512  -5.743  53.100  1.00 48.66      AAAA C
ATOM   1406  CE  LYS   143      25.043  -7.131  53.558  1.00 38.35      AAAA C
ATOM   1407  NZ  LYS   143      26.080  -8.093  53.040  1.00 53.83      AAAA N
ATOM   1411  C   LYS   143      22.902  -2.431  54.169  1.00 52.85      AAAA C
ATOM   1412  O   LYS   143      22.960  -2.099  55.360  1.00 55.21      AAAA O
ATOM   1413  N   PRO   144      21.806  -3.047  53.731  1.00 52.39      AAAA N
ATOM   1414  CD  PRO   144      21.617  -3.469  52.315  1.00 52.58      AAAA C
ATOM   1415  CA  PRO   144      20.559  -3.118  54.489  1.00 48.30      AAAA C
ATOM   1416  CB  PRO   144      19.549  -3.602  53.455  1.00 51.41      AAAA C
ATOM   1417  CG  PRO   144      20.134  -3.299  52.099  1.00 50.41      AAAA C
ATOM   1418  C   PRO   144      20.621  -4.050  55.659  1.00 44.65      AAAA C
ATOM   1419  O   PRO   144      20.904  -5.236  55.501  1.00 36.84      AAAA O
ATOM   1420  N   PRO   145      20.318  -3.533  56.859  1.00 45.12      AAAA N
ATOM   1421  CD  PRO   145      20.123  -2.054  57.094  1.00 38.17      AAAA C
ATOM   1422  CA  PRO   145      20.448  -4.233  58.128  1.00 40.19      AAAA C
ATOM   1423  CB  PRO   145      19.704  -3.288  59.099  1.00 37.08      AAAA C
ATOM   1424  CG  PRO   145      20.040  -1.910  58.602  1.00 33.65      AAAA C
ATOM   1425  C   PRO   145      19.993  -5.655  58.155  1.00 47.17      AAAA C
ATOM   1426  O   PRO   145      20.556  -6.592  58.768  1.00 48.05      AAAA O
ATOM   1427  N   LYS   146      18.879  -5.924  57.489  1.00 53.72      AAAA N
ATOM   1429  CA  LYS   146      18.268  -7.229  57.295  1.00 56.94      AAAA C
ATOM   1430  CB  LYS   146      16.894  -7.050  56.647  1.00 65.44      AAAA C
ATOM   1431  CG  LYS   146      16.220  -8.232  55.982  1.00 64.32      AAAA C
ATOM   1432  CD  LYS   146      14.797  -8.422  56.451  0.01 62.75      AAAA C
ATOM   1433  CE  LYS   146      14.194  -9.717  55.934  0.01 62.14      AAAA C
ATOM   1434  NZ  LYS   146      12.720  -9.610  55.753  0.01 61.38      AAAA N
ATOM   1438  C   LYS   146      19.138  -8.138  56.446  1.00 61.40      AAAA C
ATOM   1439  O   LYS   146      19.237  -9.346  56.732  1.00 66.22      AAAA O
ATOM   1440  N   GLU   147      19.779  -7.649  55.389  1.00 62.92      AAAA N
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ATOM   1443  CB  GLU   147      21.101  -8.070  53.294  1.00 62.32      AAAA C
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ATOM   1447  OE2 GLU   147      19.201  -7.053  50.376  1.00 87.47      AAAA O
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ATOM   1449  O   GLU   147      22.883  -9.437  55.361  1.00 72.86      AAAA O
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ATOM   1452  CA  CYS   148      23.693  -7.588  57.183  1.00 64.65      AAAA C
ATOM   1453  C   CYS   148      23.598  -8.702  58.196  1.00 65.56      AAAA C
ATOM   1454  O   CYS   148      24.473  -9.524  58.414  1.00 65.89      AAAA O
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ATOM   1474  CB  LEU   151      25.208 -11.409  65.806  1.00 58.55      AAAA C
ATOM   1475  CG  LEU   151      24.063 -12.101  65.092  1.00 69.45      AAAA C
ATOM   1476  CD1 LEU   151      24.515 -13.421  64.489  1.00 65.26      AAAA C
ATOM   1477  CD2 LEU   151      22.837 -12.372  65.951  1.00 65.43      AAAA C
ATOM   1478  C   LEU   151      26.409  -9.454  66.805  1.00 51.93      AAAA C
ATOM   1479  O   LEU   151      27.598  -9.734  66.634  1.00 55.59      AAAA O
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ATOM   1486  SG  CYS   152      25.985  -5.635  68.703  1.00 55.83      AAAA S
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ATOM   1489  CA  PRO   153      29.497 -10.094  70.851  1.00 70.60      AAAA C
ATOM   1490  CB  PRO   153      30.601  -9.323  71.557  1.00 69.98      AAAA C
ATOM   1491  CG  PRO   153      30.961  -8.159  70.690  1.00 70.58      AAAA C
ATOM   1492  C   PRO   153      28.543 -10.734  71.850  1.00 69.64      AAAA C
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ATOM   1502  CB  THR   155      24.016 -11.661  69.705  1.00 85.07      AAAA C
ATOM   1503  OG1 THR   155      24.063 -10.417  70.420  1.00 84.51      AAAA O
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ATOM   1512  CG  MET   156      25.456 -15.675  66.542  0.01 99.75      AAAA C
ATOM   1513  SD  MET   156      23.687 -15.857  66.255  0.01 99.72      AAAA S
ATOM   1514  CE  MET   156      23.664 -17.214  65.087  0.01 99.59      AAAA C
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ATOM   1527  CG  GLU   158      21.687 -17.546  75.560  1.00113.87      AAAA C
ATOM   1528  CD  GLU   158      21.347 -16.081  75.302  1.00119.34      AAAA C
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ATOM   1530  OE2 GLU   158      21.199 -15.317  76.282  1.00117.79      AAAA O
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ATOM   1552  CG  MET   161      30.118 -10.630  75.706  1.00 71.43      AAAA C
ATOM   1553  SD  MET   161      30.716 -11.621  77.094  1.00 85.25      AAAA S
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ATOM   1571  OE2 GLU   163      24.646   0.208  78.721  1.00 80.93      AAAA O
ATOM   1572  C   GLU   163      24.299  -2.340  75.472  1.00 49.05      AAAA C
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ATOM   1590  CB  THR   165      21.831   2.952  73.553  1.00 47.81      AAAA C
ATOM   1591  OG1 THR   165      22.053   2.689  72.127  1.00 39.13      AAAA O
ATOM   1593  CG2 THR   165      23.119   2.842  74.362  1.00 40.40      AAAA C
ATOM   1594  C   THR   165      19.532   1.881  73.189  1.00 40.92      AAAA C
ATOM   1595  O   THR   165      19.346   0.897  72.414  1.00 35.91      AAAA O
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ATOM   1598  CA  THR   166      17.689   2.991  72.182  1.00 42.97      AAAA C
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ATOM   1608  CB  ILE   167      19.437   4.335  67.904  1.00 39.50      AAAA C
ATOM   1609  CG2 ILE   167      19.589   5.346  66.716  1.00 15.26      AAAA C
ATOM   1610  CG1 ILE   167      20.722   4.305  68.724  1.00 36.20      AAAA C
ATOM   1611  CD1 ILE   167      21.899   3.665  67.966  1.00 35.70      AAAA C
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ATOM   1642  OE1 GLU   170      13.869   0.466  65.049  1.00 77.75      AAAA O
ATOM   1643  OE2 GLU   170      14.763  -1.437  64.389  1.00 70.71      AAAA O
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ATOM   1650  CG  TYR   171      16.175  -1.168  74.620  1.00 48.90      AAAA C
ATOM   1651  CD1 TYR   171      16.980  -0.210  75.237  1.00 46.46      AAAA C
ATOM   1652  CE1 TYR   171      17.634  -0.469  76.407  1.00 41.17      AAAA C
ATOM   1653  CD2 TYR   171      16.065  -2.429  75.194  1.00 43.62      AAAA C
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ATOM   1655  CZ  TYR   171      17.516  -1.718  76.973  1.00 43.58      AAAA C
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ATOM   1658  C   TYR   171      17.058  -1.938  71.832  1.00 51.41      AAAA C
ATOM   1659  O   TYR   171      16.519  -3.024  71.889  1.00 52.59      AAAA O
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ATOM   1676  CD1 TYR   173      21.931  -7.316  72.237  1.00 46.48      AAAA C
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ATOM   1678  CD2 TYR   173      23.081  -6.132  73.978  1.00 44.86      AAAA C
ATOM   1679  CE2 TYR   173      22.583  -7.016  74.916  1.00 46.92      AAAA C
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ATOM   1687  CA  ARG   174      25.517  -1.496  70.577  1.00 49.13      AAAA C
ATOM   1688  CB  ARG   174      25.537  -0.132  71.233  1.00 44.32      AAAA C
ATOM   1689  CG  ARG   174      24.210   0.623  71.234  1.00 48.14      AAAA C
ATOM   1690  CD  ARG   174      23.372   0.344  70.003  1.00 51.47      AAAA C
ATOM   1691  NE  ARG   174      21.974   0.760  70.039  1.00 48.35      AAAA N
ATOM   1693  CZ  ARG   174      21.144   0.570  69.017  1.00 48.23      AAAA C
ATOM   1694  NH1 ARG   174      21.477   0.022  67.864  1.00 38.96      AAAA N
ATOM   1697  NH2 ARG   174      19.909   1.022  69.197  1.00 54.65      AAAA N
ATOM   1700  C   ARG   174      26.921  -2.094  70.461  1.00 45.98      AAAA C
ATOM   1701  O   ARG   174      27.548  -2.557  71.406  1.00 44.97      AAAA O
ATOM   1702  N   CYS   175      27.493  -2.183  69.294  1.00 46.21      AAAA N
ATOM   1704  CA  CYS   175      28.787  -2.758  68.997  1.00 45.60      AAAA C
ATOM   1705  C   CYS   175      29.407  -2.395  67.665  1.00 46.23      AAAA C
ATOM   1706  O   CYS   175      28.755  -2.018  66.665  1.00 44.78      AAAA O
ATOM   1707  CB  CYS   175      28.576  -4.253  69.167  1.00 35.62      AAAA C
ATOM   1708  SG  CYS   175      27.812  -5.181  67.827  1.00 51.92      AAAA S
ATOM   1709  N   TRP   176      30.764  -2.517  67.583  1.00 48.16      AAAA N
ATOM   1711  CA  TRP   176      31.430  -2.091  66.325  1.00 42.48      AAAA C
ATOM   1712  CB  TRP   176      32.769  -1.409  66.564  1.00 36.38      AAAA C
ATOM   1713  CG  TRP   176      32.689  -0.069  67.203  1.00 25.56      AAAA C
ATOM   1714  CD2 TRP   176      32.588   1.186  66.489  1.00 23.71      AAAA C
ATOM   1715  CE2 TRP   176      32.559   2.217  67.422  1.00 32.40      AAAA C
ATOM   1716  CE3 TRP   176      32.535   1.520  65.141  1.00 24.31      AAAA C
ATOM   1717  CD1 TRP   176      32.730   0.257  68.525  1.00 28.37      AAAA C
ATOM   1718  NE1 TRP   176      32.636   1.636  68.678  1.00 37.21      AAAA N
ATOM   1720  CZ2 TRP   176      32.441   3.565  67.088  1.00 28.51      AAAA C
ATOM   1721  CZ3 TRP   176      32.447   2.822  64.789  1.00 22.23      AAAA C
ATOM   1722  CH2 TRP   176      32.406   3.817  65.745  1.00 29.51      AAAA C
ATOM   1723  C   TRP   176      31.631  -3.268  65.408  1.00 39.30      AAAA C
ATOM   1724  O   TRP   176      31.703  -3.121  64.199  1.00 39.15      AAAA O
ATOM   1725  N   THR   177      31.682  -4.460  66.005  1.00 41.33      AAAA N
ATOM   1727  CA  THR   177      31.964  -5.644  65.161  1.00 49.28      AAAA C
ATOM   1728  CB  THR   177      33.480  -6.062  65.162  1.00 43.66      AAAA C
ATOM   1729  OG1 THR   177      34.309  -5.025  64.613  1.00 47.85      AAAA O
ATOM   1731  CG2 THR   177      33.676  -7.271  64.283  1.00 58.51      AAAA C
ATOM   1732  C   THR   177      31.290  -6.814  65.858  1.00 48.76      AAAA C
ATOM   1733  O   THR   177      30.982  -6.539  67.001  1.00 51.53      AAAA O
ATOM   1734  N   THR   178      31.269  -8.000  65.331  1.00 51.96      AAAA N
ATOM   1736  CA  THR   178      30.924  -9.236  65.946  1.00 58.95      AAAA C
ATOM   1737  CB  THR   178      31.253 -10.500  65.082  1.00 66.55      AAAA C
ATOM   1738  OG1 THR   178      31.505 -10.066  63.734  1.00 75.70      AAAA O
ATOM   1740  CG2 THR   178      30.104 -11.489  65.148  1.00 74.23      AAAA C
ATOM   1741  C   THR   178      31.714  -9.539  67.213  1.00 60.25      AAAA C
ATOM   1742  O   THR   178      31.204 -10.202  68.135  1.00 66.05      AAAA O
ATOM   1743  N   ASN   179      32.977  -9.130  67.253  1.00 57.56      AAAA N
ATOM   1745  CA  ASN   179      33.793  -9.392  68.443  1.00 53.39      AAAA C
ATOM   1746  CB  ASN   179      35.130 -10.024  68.068  1.00 48.46      AAAA C
ATOM   1747  CG  ASN   179      34.997 -11.218  67.126  1.00 56.25      AAAA C
ATOM   1748  OD1 ASN   179      34.412 -12.294  67.553  1.00 51.38      AAAA O
ATOM   1749  ND2 ASN   179      35.229 -11.063  65.863  1.00 48.10      AAAA N
ATOM   1752  C   ASN   179      34.096  -8.129  69.288  1.00 50.78      AAAA C
ATOM   1753  O   ASN   179      34.556  -8.377  70.426  1.00 57.97      AAAA O
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ATOM   1754  N   ARG   180      33.626  -7.022  68.913  1.00 47.06      AAAA N
ATOM   1756  CA  ARG   180      33.808  -5.820  69.691  1.00 48.25      AAAA C
ATOM   1757  CB  ARG   180      34.925  -4.962  69.074  1.00 49.72      AAAA C
ATOM   1758  CG  ARG   180      36.324  -5.501  69.285  1.00 60.92      AAAA C
ATOM   1759  CD  ARG   180      37.288  -4.948  68.279  1.00 70.83      AAAA C
ATOM   1760  NE  ARG   180      38.569  -5.605  68.203  1.00 76.18      AAAA N
ATOM   1762  CZ  ARG   180      39.298  -5.895  69.276  1.00 76.59      AAAA C
ATOM   1763  NH1 ARG   180      38.877  -5.608  70.498  1.00 80.82      AAAA N
ATOM   1766  NH2 ARG   180      40.474  -6.478  69.180  1.00 79.33      AAAA N
ATOM   1769  C   ARG   180      32.530  -4.977  69.821  1.00 48.10      AAAA C
ATOM   1770  O   ARG   180      31.862  -4.476  68.905  1.00 46.99      AAAA O
ATOM   1771  N   CYS   181      32.230  -4.728  71.063  1.00 44.80      AAAA N
ATOM   1773  CA  CYS   181      31.199  -3.924  71.619  1.00 45.20      AAAA C
ATOM   1774  C   CYS   181      31.646  -2.463  71.692  1.00 44.50      AAAA C
ATOM   1775  O   CYS   181      32.835  -2.227  71.724  1.00 47.09      AAAA O
ATOM   1776  CB  CYS   181      30.940  -4.282  73.110  1.00 43.88      AAAA C
ATOM   1777  SG  CYS   181      30.363  -5.944  73.346  1.00 56.08      AAAA S
ATOM   1778  N   GLN   182      30.659  -1.600  71.690  1.00 39.30      AAAA N
ATOM   1780  CA  GLN   182      30.948  -0.177  71.690  1.00 43.43      AAAA C
ATOM   1781  CB  GLN   182      29.749   0.619  71.196  1.00 23.99      AAAA C
ATOM   1782  CG  GLN   182      29.809   2.085  71.435  1.00 28.57      AAAA C
ATOM   1783  CD  GLN   182      28.757   2.867  70.733  1.00 29.35      AAAA C
ATOM   1784  OE1 GLN   182      27.898   2.304  70.033  1.00 38.55      AAAA O
ATOM   1785  NE2 GLN   182      28.857   4.164  70.912  1.00 28.14      AAAA N
ATOM   1788  C   GLN   182      31.218   0.089  73.162  1.00 46.07      AAAA C
ATOM   1789  O   GLN   182      30.458  -0.327  74.041  1.00 47.01      AAAA O
ATOM   1790  N   LYS   183      32.213   0.866  73.524  1.00 46.98      AAAA N
ATOM   1792  CA  LYS   183      32.479   1.064  74.934  1.00 45.26      AAAA C
ATOM   1793  CB  LYS   183      33.966   1.275  75.185  1.00 48.68      AAAA C
ATOM   1794  CG  LYS   183      34.865   0.267  74.482  1.00 47.95      AAAA C
ATOM   1795  CD  LYS   183      36.337   0.734  74.523  1.00 48.06      AAAA C
ATOM   1796  CE  LYS   183      37.178  -0.208  73.684  1.00 46.78      AAAA C
ATOM   1797  NZ  LYS   183      38.499  -0.654  74.158  1.00 44.00      AAAA N
ATOM   1801  C   LYS   183      31.659   2.205  75.477  1.00 48.13      AAAA C
ATOM   1802  O   LYS   183      31.679   3.305  74.946  1.00 48.84      AAAA O
ATOM   1803  N   MET   184      31.165   2.014  76.698  1.00 52.59      AAAA N
ATOM   1805  CA  MET   184      30.388   3.041  77.413  1.00 53.22      AAAA C
ATOM   1806  CB  MET   184      28.927   2.613  77.537  1.00 54.27      AAAA C
ATOM   1807  CG  MET   184      27.855   2.955  76.536  1.00 56.16      AAAA C
ATOM   1808  SD  MET   184      26.911   1.601  75.912  1.00 57.56      AAAA S
ATOM   1809  CE  MET   184      26.738   1.855  74.171  1.00 46.57      AAAA C
ATOM   1810  C   MET   184      31.051   3.200  78.770  1.00 50.55      AAAA C
ATOM   1811  O   MET   184      31.770   2.292  79.116  1.00 48.82      AAAA O
ATOM   1812  N   CYS   185      30.796   4.195  79.565  1.00 53.97      AAAA N
ATOM   1814  CA  CYS   185      31.342   4.365  80.892  1.00 58.63      AAAA C
ATOM   1815  C   CYS   185      30.297   4.320  81.989  1.00 65.16      AAAA C
ATOM   1816  O   CYS   185      29.133   4.649  81.761  1.00 65.87      AAAA O
ATOM   1817  CB  CYS   185      31.965   5.772  81.000  1.00 60.37      AAAA C
ATOM   1818  SG  CYS   185      33.623   5.771  80.312  1.00 60.09      AAAA S
ATOM   1819  N   PRO   186      30.688   3.978  83.206  1.00 69.41      AAAA N
ATOM   1820  CD  PRO   186      32.066   3.777  83.702  1.00 71.11      AAAA C
ATOM   1821  CA  PRO   186      29.717   3.933  84.304  1.00 69.11      AAAA C
ATOM   1822  CB  PRO   186      30.523   3.487  85.503  1.00 68.03      AAAA C
ATOM   1823  CG  PRO   186      31.910   3.920  85.198  1.00 71.02      AAAA C
ATOM   1824  C   PRO   186      29.120   5.320  84.431  1.00 69.47      AAAA C
ATOM   1825  O   PRO   186      29.820   6.345  84.507  1.00 65.93      AAAA O
ATOM   1826  N   SER   187      27.801   5.367  84.546  1.00 68.78      AAAA N
ATOM   1828  CA  SER   187      27.050   6.592  84.750  1.00 69.29      AAAA C
ATOM   1829  CB  SER   187      25.594   6.287  85.129  1.00 78.29      AAAA C
ATOM   1830  OG  SER   187      25.474   4.935  85.566  1.00 91.78      AAAA O
ATOM   1832  C   SER   187      27.630   7.476  85.836  1.00 67.19      AAAA C
ATOM   1833  O   SER   187      27.606   8.708  85.803  1.00 63.98      AAAA O
ATOM   1834  N   THR   188      28.108   6.853  86.908  1.00 68.20      AAAA N
ATOM   1836  CA  THR   188      28.870   7.507  87.963  1.00 68.39      AAAA C
ATOM   1837  CB  THR   188      29.805   6.459  88.618  1.00 73.84      AAAA C
ATOM   1838  OG1 THR   188      28.943   5.365  89.016  1.00 89.33      AAAA O
ATOM   1840  CG2 THR   188      30.605   7.048  89.759  1.00 73.71      AAAA C
ATOM   1841  C   THR   188      29.802   8.583  87.429  1.00 67.52      AAAA C
ATOM   1842  O   THR   188      29.843   9.739  87.834  1.00 68.30      AAAA O
ATOM   1843  N   CYS   189      30.643   8.247  86.446  1.00 63.89      AAAA N
ATOM   1845  CA  CYS   189      31.583   9.116  85.817  1.00 57.29      AAAA C
ATOM   1846  C   CYS   189      30.951  10.331  85.195  1.00 57.70      AAAA C
ATOM   1847  O   CYS   189      31.648  11.327  85.017  1.00 57.56      AAAA O
ATOM   1848  CB  CYS   189      32.416   8.372  84.769  1.00 58.67      AAAA C
ATOM   1849  SG  CYS   189      33.347   7.001  85.535  1.00 53.46      AAAA S
ATOM   1850  N   GLY   190      29.689  10.322  84.806  1.00 56.91      AAAA N
ATOM   1852  CA  GLY   190      29.038  11.521  84.323  1.00 57.28      AAAA C
ATOM   1853  C   GLY   190      29.444  11.834  82.886  1.00 59.62      AAAA C
ATOM   1854  O   GLY   190      29.609  10.932  82.082  1.00 57.91      AAAA O
ATOM   1855  N   LYS   191      29.842  13.052  82.624  1.00 62.78      AAAA N
ATOM   1857  CA  LYS   191      30.359  13.520  81.364  1.00 67.72      AAAA C
ATOM   1858  CB  LYS   191      30.058  15.035  81.214  1.00 72.76      AAAA C
ATOM   1859  CG  LYS   191      28.568  15.288  81.002  1.00 84.69      AAAA C
ATOM   1860  CD  LYS   191      28.207  16.733  80.723  1.00 90.15      AAAA C
ATOM   1861  CE  LYS   191      26.713  16.806  80.471  1.00 91.83      AAAA C
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ATOM   1862  ND2 LYS   191      26.368  16.182  79.152  1.00 97.62      AAAA N
ATOM   1866  C   LYS   191      31.868  13.299  81.270  1.00 70.13      AAAA C
ATOM   1867  O   LYS   191      32.486  13.935  80.415  1.00 71.76      AAAA O
ATOM   1868  N   ARG   192      32.488  12.441  82.079  1.00 66.29      AAAA N
ATOM   1870  CA  ARG   192      33.885  12.171  82.044  1.00 59.95      AAAA C
ATOM   1871  CB  ARG   192      34.505  12.070  83.432  1.00 66.58      AAAA C
ATOM   1872  CG  ARG   192      34.670  13.400  84.131  1.00 71.59      AAAA C
ATOM   1873  CD  ARG   192      34.386  13.330  85.625  1.00 73.91      AAAA C
ATOM   1874  NE  ARG   192      35.622  13.280  86.377  1.00 85.74      AAAA N
ATOM   1876  CZ  ARG   192      35.968  12.407  87.330  1.00 90.67      AAAA C
ATOM   1877  NH1 ARG   192      35.026  11.486  87.600  1.00 88.49      AAAA N
ATOM   1880  NH2 ARG   192      37.162  12.463  87.950  1.00 72.95      AAAA N
ATOM   1883  C   ARG   192      34.221  10.851  81.337  1.00 58.83      AAAA C
ATOM   1884  O   ARG   192      33.336  10.007  81.176  1.00 55.13      AAAA O
ATOM   1885  N   ALA   193      35.521  10.795  80.968  1.00 50.19      AAAA N
ATOM   1887  CA  ALA   193      35.962   9.557  80.355  1.00 46.24      AAAA C
ATOM   1888  CB  ALA   193      37.167   9.921  79.541  1.00 45.18      AAAA C
ATOM   1889  C   ALA   193      36.221   8.525  81.451  1.00 48.97      AAAA C
ATOM   1890  O   ALA   193      36.220   8.908  82.616  1.00 44.80      AAAA O
ATOM   1891  N   CYS   194      36.544   7.304  81.065  1.00 50.30      AAAA N
ATOM   1893  CA  CYS   194      36.836   6.302  82.043  1.00 57.50      AAAA C
ATOM   1894  C   CYS   194      37.834   5.304  81.448  1.00 61.25      AAAA C
ATOM   1895  O   CYS   194      37.952   5.291  80.216  1.00 61.52      AAAA O
ATOM   1896  CB  CYS   194      35.510   5.741  82.504  1.00 57.96      AAAA C
ATOM   1897  SG  CYS   194      34.785   4.524  81.402  1.00 54.49      AAAA S
ATOM   1898  N   THR   195      38.422   4.499  82.311  1.00 58.51      AAAA N
ATOM   1900  CA  THR   195      39.462   3.584  81.913  1.00 57.42      AAAA C
ATOM   1901  CB  THR   195      40.237   3.142  83.188  1.00 65.73      AAAA C
ATOM   1902  OG1 THR   195      40.288   4.248  84.091  1.00 70.15      AAAA O
ATOM   1904  CG2 THR   195      41.684   2.864  82.745  1.00 77.91      AAAA C
ATOM   1905  C   THR   195      38.857   2.404  81.226  1.00 54.59      AAAA C
ATOM   1906  O   THR   195      37.633   2.315  81.318  1.00 58.75      AAAA O
ATOM   1907  N   GLU   196      39.610   1.408  80.882  1.00 55.95      AAAA N
ATOM   1909  CA  GLU   196      39.139   0.145  80.364  1.00 60.07      AAAA C
ATOM   1910  CB  GLU   196      40.395  -0.612  79.914  1.00 68.06      AAAA C
ATOM   1911  CG  GLU   196      40.479  -1.146  78.526  1.00 73.96      AAAA C
ATOM   1912  CD  GLU   196      39.235  -0.983  77.670  1.00 83.08      AAAA C
ATOM   1913  OE1 GLU   196      38.356  -1.884  77.687  1.00 81.19      AAAA O
ATOM   1914  OE2 GLU   196      39.060   0.041  76.939  1.00 82.10      AAAA O
ATOM   1915  C   GLU   196      38.382  -0.579  81.467  1.00 63.91      AAAA C
ATOM   1916  O   GLU   196      37.690  -1.537  81.159  1.00 63.51      AAAA O
ATOM   1917  N   ASN   197      38.666  -0.312  82.739  1.00 67.40      AAAA N
ATOM   1919  CA  ASN   197      38.025  -0.947  83.886  1.00 69.21      AAAA C
ATOM   1920  CB  ASN   197      39.021  -1.394  84.966  1.00 68.49      AAAA C
ATOM   1921  CG  ASN   197      39.722  -2.692  84.672  0.01 69.09      AAAA C
ATOM   1922  OD1 ASN   197      40.364  -3.273  85.551  0.01 69.04      AAAA O
ATOM   1923  ND2 ASN   197      39.622  -3.183  83.443  0.01 68.97      AAAA N
ATOM   1926  C   ASN   197      37.033   0.043  84.486  1.00 69.01      AAAA C
ATOM   1927  O   ASN   197      36.845   0.281  85.664  1.00 68.24      AAAA O
ATOM   1928  N   ASN   198      36.384   0.795  83.607  1.00 69.91      AAAA N
ATOM   1930  CA  ASN   198      35.356   1.734  84.048  1.00 68.48      AAAA C
ATOM   1931  CB  ASN   198      34.120   0.880  84.373  1.00 60.12      AAAA C
ATOM   1932  CG  ASN   198      33.806   0.095  83.102  1.00 69.29      AAAA C
ATOM   1933  OD1 ASN   198      33.475   0.654  82.054  1.00 73.20      AAAA O
ATOM   1934  ND2 ASN   198      33.980  -1.206  83.268  1.00 65.34      AAAA N
ATOM   1937  C   ASN   198      35.784   2.563  85.228  1.00 64.01      AAAA C
ATOM   1938  O   ASN   198      34.992   2.827  86.117  1.00 64.20      AAAA O
ATOM   1939  N   GLU   199      36.955   3.164  85.157  1.00 64.75      AAAA N
ATOM   1941  CA  GLU   199      37.342   4.054  86.255  1.00 64.64      AAAA C
ATOM   1942  CB  GLU   199      38.702   3.624  86.744  1.00 66.11      AAAA C
ATOM   1943  CG  GLU   199      38.846   3.717  88.233  1.00 77.15      AAAA C
ATOM   1944  CD  GLU   199      39.579   2.532  88.832  1.00 80.24      AAAA C
ATOM   1945  OE1 GLU   199      39.385   2.406  90.066  1.00 81.65      AAAA O
ATOM   1946  OE2 GLU   199      40.282   1.821  88.079  1.00 77.94      AAAA O
ATOM   1947  C   GLU   199      37.314   5.463  85.690  1.00 62.92      AAAA C
ATOM   1948  O   GLU   199      37.922   5.676  84.632  1.00 63.62      AAAA O
ATOM   1949  N   CYS   200      36.605   6.393  86.313  1.00 56.16      AAAA N
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ATOM   1952  C   CYS   200      37.978   8.315  85.521  1.00 57.77      AAAA C
ATOM   1953  O   CYS   200      38.884   8.058  86.300  1.00 63.79      AAAA O
ATOM   1954  CB  CYS   200      35.824   8.664  86.648  1.00 52.70      AAAA C
ATOM   1955  SG  CYS   200      34.196   8.100  87.098  1.00 55.85      AAAA S
ATOM   1956  N   CYS   201      38.124   9.192  84.540  1.00 54.50      AAAA N
ATOM   1958  CA  CYS   201      39.338   9.889  84.202  1.00 48.19      AAAA C
ATOM   1959  C   CYS   201      39.236  11.287  84.786  1.00 42.34      AAAA C
ATOM   1960  O   CYS   201      38.165  11.704  85.166  1.00 54.32      AAAA O
ATOM   1961  CB  CYS   201      39.590  10.070  82.695  1.00 40.90      AAAA C
ATOM   1962  SG  CYS   201      39.644   8.597  81.747  1.00 51.42      AAAA S
ATOM   1963  N   HIS   202      40.254  12.075  84.675  1.00 39.12      AAAA N
ATOM   1965  CA  HIS   202      40.290  13.461  85.128  1.00 41.55      AAAA C
ATOM   1966  C   HIS   202      39.284  14.184  84.289  1.00 46.59      AAAA C
ATOM   1967  O   HIS   202      39.176  13.851  83.103  1.00 51.64      AAAA O
ATOM   1968  CB  HIS   202      41.712  13.952  84.810  1.00 45.20      AAAA C
ATOM   1969  CG  HIS   202      41.996  15.330  85.267  1.00 38.71      AAAA C
ATOM   1970  ND1 HIS   202      41.501  16.404  84.550  1.00 51.32      AAAA N
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ATOM   1971  CE1 HIS   202      41.887  17.528  85.178  1.00 47.62      AAAA C
ATOM   1972  CD2 HIS   202      42.665  15.813  86.340  1.00 39.59      AAAA C
ATOM   1973  NE2 HIS   202      42.563  17.207  86.258  1.00 43.48      AAAA N
ATOM   1975  N   PRO   203      38.738  15.293  84.711  1.00 47.74      AAAA N
ATOM   1976  CD  PRO   203      38.758  15.840  86.082  1.00 46.97      AAAA C
ATOM   1977  CA  PRO   203      37.780  15.987  83.879  1.00 46.44      AAAA C
ATOM   1978  CB  PRO   203      37.248  17.107  84.742  1.00 39.47      AAAA C
ATOM   1979  CG  PRO   203      38.131  17.210  85.910  1.00 43.37      AAAA C
ATOM   1980  C   PRO   203      38.440  16.519  82.607  1.00 53.27      AAAA C
ATOM   1981  O   PRO   203      37.698  17.045  81.731  1.00 53.16      AAAA O
ATOM   1982  N   GLU   204      39.792  16.535  82.561  1.00 50.34      AAAA N
ATOM   1984  CA  GLU   204      40.439  17.139  81.381  1.00 50.52      AAAA C
ATOM   1985  CB  GLU   204      41.727  17.891  81.804  1.00 48.58      AAAA C
ATOM   1986  CG  GLU   204      41.397  19.251  82.397  1.00 43.74      AAAA C
ATOM   1987  CD  GLU   204      40.778  20.282  81.501  1.00 55.26      AAAA C
ATOM   1988  OE1 GLU   204      40.766  20.344  80.248  1.00 64.04      AAAA O
ATOM   1989  OE2 GLU   204      40.226  21.198  82.141  1.00 57.66      AAAA O
ATOM   1990  C   GLU   204      40.718  16.084  80.319  1.00 45.71      AAAA C
ATOM   1991  O   GLU   204      41.238  16.405  79.251  1.00 46.56      AAAA O
ATOM   1992  N   CYS   205      40.612  14.830  80.735  1.00 42.05      AAAA N
ATOM   1994  CA  CYS   205      40.997  13.764  79.838  1.00 45.81      AAAA C
ATOM   1995  C   CYS   205      39.892  13.628  78.819  1.00 49.20      AAAA C
ATOM   1996  O   CYS   205      38.746  13.920  79.133  1.00 50.34      AAAA O
ATOM   1997  CB  CYS   205      41.288  12.491  80.572  1.00 51.55      AAAA C
ATOM   1998  SG  CYS   205      42.923  12.246  81.251  1.00 52.89      AAAA S
ATOM   1999  N   LEU   206      40.232  13.579  77.520  1.00 49.88      AAAA N
ATOM   2001  CA  LEU   206      39.169  13.446  76.533  1.00 41.49      AAAA C
ATOM   2002  CB  LEU   206      39.266  14.505  75.462  1.00 48.66      AAAA C
ATOM   2003  CG  LEU   206      38.274  14.365  74.305  1.00 47.45      AAAA C
ATOM   2004  CD1 LEU   206      36.879  14.243  74.895  1.00 45.79      AAAA C
ATOM   2005  CD2 LEU   206      38.331  15.599  73.420  1.00 50.71      AAAA C
ATOM   2006  C   LEU   206      39.310  12.109  75.912  1.00 38.44      AAAA C
ATOM   2007  O   LEU   206      40.400  11.568  75.813  1.00 36.59      AAAA O
ATOM   2008  N   GLY   207      38.264  11.359  75.681  1.00 42.41      AAAA N
ATOM   2010  CA  GLY   207      38.403  10.098  74.978  1.00 40.57      AAAA C
ATOM   2011  C   GLY   207      38.466   9.061  76.058  1.00 47.15      AAAA C
ATOM   2012  O   GLY   207      37.668   8.102  76.057  1.00 45.04      AAAA O
ATOM   2013  N   SER   208      39.622   9.079  76.760  1.00 50.36      AAAA N
ATOM   2015  CA  SER   208      39.832   7.898  77.660  1.00 48.27      AAAA C
ATOM   2016  CB  SER   208      39.909   6.631  76.787  1.00 35.77      AAAA C
ATOM   2017  OG  SER   208      40.600   5.597  77.461  1.00 61.34      AAAA O
ATOM   2019  C   SER   208      41.144   8.068  78.377  1.00 49.17      AAAA C
ATOM   2020  O   SER   208      41.781   9.084  78.163  1.00 48.24      AAAA O
ATOM   2021  N   CYS   209      41.599   7.123  79.189  1.00 52.04      AAAA N
ATOM   2023  CA  CYS   209      42.824   7.307  79.964  1.00 55.98      AAAA C
ATOM   2024  C   CYS   209      43.453   6.035  80.484  1.00 57.41      AAAA C
ATOM   2025  O   CYS   209      42.862   4.963  80.423  1.00 58.33      AAAA O
ATOM   2026  CB  CYS   209      42.629   8.258  81.146  1.00 52.51      AAAA C
ATOM   2027  SG  CYS   209      41.380   7.602  82.261  1.00 58.22      AAAA S
ATOM   2028  N   SER   210      44.734   6.145  80.883  1.00 59.37      AAAA N
ATOM   2030  CA  SER   210      45.506   4.950  81.318  1.00 58.10      AAAA C
ATOM   2031  CB  SER   210      47.022   5.083  81.105  1.00 55.07      AAAA C
ATOM   2032  OG  SER   210      47.546   6.204  81.818  1.00 64.49      AAAA O
ATOM   2034  C   SER   210      45.331   4.713  82.826  1.00 56.34      AAAA C
ATOM   2035  O   SER   210      45.529   3.614  83.326  1.00 54.42      AAAA O
ATOM   2036  N   ALA   211      45.105   5.806  83.548  1.00 52.79      AAAA N
ATOM   2038  CA  ALA   211      44.980   5.684  85.004  1.00 56.60      AAAA C
ATOM   2039  CB  ALA   211      46.333   5.926  85.649  1.00 63.41      AAAA C
ATOM   2040  C   ALA   211      43.962   6.747  85.395  1.00 56.58      AAAA C
ATOM   2041  O   ALA   211      43.957   7.792  84.711  1.00 50.78      AAAA O
ATOM   2042  N   PRO   212      43.117   6.416  86.359  1.00 55.93      AAAA N
ATOM   2043  CD  PRO   212      43.042   5.166  87.115  1.00 55.86      AAAA C
ATOM   2044  CA  PRO   212      41.951   7.257  86.575  1.00 55.50      AAAA C
ATOM   2045  CB  PRO   212      41.104   6.470  87.556  1.00 59.65      AAAA C
ATOM   2046  CG  PRO   212      42.021   5.483  88.175  1.00 54.56      AAAA C
ATOM   2047  C   PRO   212      42.409   8.535  87.177  1.00 53.64      AAAA C
ATOM   2048  O   PRO   212      43.611   8.725  87.393  1.00 57.46      AAAA O
ATOM   2049  N   ALA   213      41.537   9.492  87.347  1.00 53.87      AAAA N
ATOM   2051  CA  ALA   213      41.912  10.710  88.057  1.00 59.41      AAAA C
ATOM   2052  CB  ALA   213      41.783  10.255  89.541  1.00 66.40      AAAA C
ATOM   2053  C   ALA   213      43.289  11.300  87.907  1.00 61.40      AAAA C
ATOM   2054  O   ALA   213      43.728  12.202  88.652  1.00 60.03      AAAA O
ATOM   2055  N   ASN   214      44.068  10.999  86.899  1.00 64.80      AAAA N
ATOM   2057  CA  ASN   214      45.366  11.551  86.596  1.00 63.36      AAAA C
ATOM   2063  C   ASN   214      45.300  12.284  85.251  1.00 61.56      AAAA C
ATOM   2064  O   ASN   214      45.198  11.794  84.117  1.00 58.38      AAAA O
ATOM   2058  CB  ASN   214      46.336  10.379  86.608  1.00 67.32      AAAA C
ATOM   2059  CG  ASN   214      47.697  10.896  86.362  1.00 75.48      AAAA C
ATOM   2060  OD1 ASN   214      48.254  11.105  85.302  1.00 83.64      AAAA O
ATOM   2061  ND2 ASN   214      48.513  11.170  87.427  1.00 90.05      AAAA N
ATOM   2065  N   ASP   215      45.666  13.565  85.305  1.00 59.78      AAAA N
ATOM   2067  CA  ASP   215      45.618  14.432  84.143  1.00 56.47      AAAA C
ATOM   2068  CB  ASP   215      45.430  15.926  84.446  1.00 40.19      AAAA C
ATOM   2069  CG  ASP   215      46.671  16.543  84.986  1.00 56.36      AAAA C
ATOM   2070  OD1 ASP   215      46.590  17.699  85.473  1.00 56.17      AAAA O
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ATOM   2071  OD2 ASP   215      47.766  15.926  84.941  1.00 60.51      AAAA O
ATOM   2072  C   ASP   215      46.818  14.315  83.221  1.00 53.78      AAAA C
ATOM   2073  O   ASP   215      46.998  15.148  82.322  1.00 53.58      AAAA O
ATOM   2074  N   THR   216      47.719  13.425  83.511  1.00 50.87      AAAA N
ATOM   2076  CA  THR   216      48.883  13.114  82.734  1.00 45.76      AAAA C
ATOM   2077  CB  THR   216      50.201  13.176  83.529  1.00 53.46      AAAA C
ATOM   2078  OG1 THR   216      50.403  11.977  84.335  1.00 45.14      AAAA O
ATOM   2080  CG2 THR   216      50.436  14.314  84.518  1.00 41.38      AAAA C
ATOM   2081  C   THR   216      48.681  11.712  82.158  1.00 48.34      AAAA C
ATOM   2082  O   THR   216      49.596  11.282  81.444  1.00 47.49      AAAA O
ATOM   2083  N   ALA   217      47.559  11.057  82.476  1.00 49.65      AAAA N
ATOM   2085  CA  ALA   217      47.259   9.760  81.845  1.00 51.83      AAAA C
ATOM   2086  CB  ALA   217      46.908   8.775  82.943  1.00 52.62      AAAA C
ATOM   2087  C   ALA   217      46.207   9.747  80.709  1.00 50.60      AAAA C
ATOM   2088  O   ALA   217      45.775   8.632  80.335  1.00 49.13      AAAA O
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ATOM   2091  CA  CYS   218      44.802  11.030  79.157  1.00 48.09      AAAA C
ATOM   2092  C   CYS   218      45.166  10.331  77.869  1.00 47.06      AAAA C
ATOM   2093  O   CYS   218      46.300   9.967  77.642  1.00 55.57      AAAA O
ATOM   2094  CB  CYS   218      44.536  12.501  78.775  1.00 51.54      AAAA C
ATOM   2095  SG  CYS   218      44.256  13.494  80.302  1.00 56.98      AAAA S
ATOM   2096  N   VAL   219      44.226  10.085  76.978  1.00 43.40      AAAA N
ATOM   2098  CA  VAL   219      44.575   9.547  75.654  1.00 35.22      AAAA C
ATOM   2099  CB  VAL   219      43.693   8.427  75.242  1.00 32.26      AAAA C
ATOM   2100  CG1 VAL   219      43.952   7.873  73.886  1.00 36.19      AAAA C
ATOM   2101  CG2 VAL   219      43.811   7.144  76.071  1.00 45.51      AAAA C
ATOM   2102  C   VAL   219      44.453  10.750  74.735  1.00 32.06      AAAA C
ATOM   2103  O   VAL   219      45.303  10.897  73.874  1.00 42.27      AAAA O
ATOM   2104  N   ALA   220      43.728  11.759  75.187  1.00 24.24      AAAA N
ATOM   2106  CA  ALA   220      43.630  12.985  74.385  1.00 27.99      AAAA C
ATOM   2107  CB  ALA   220      42.536  12.919  73.331  1.00 28.42      AAAA C
ATOM   2108  C   ALA   220      43.292  14.071  75.390  1.00 29.21      AAAA C
ATOM   2109  O   ALA   220      42.846  13.604  76.455  1.00 37.88      AAAA O
ATOM   2110  N   CYS   221      43.285  15.334  75.058  1.00 30.27      AAAA N
ATOM   2112  CA  CYS   221      42.753  16.382  75.875  1.00 35.55      AAAA C
ATOM   2113  C   CYS   221      41.460  17.055  75.452  1.00 47.06      AAAA C
ATOM   2114  O   CYS   221      41.265  17.598  74.368  1.00 49.57      AAAA O
ATOM   2115  CB  CYS   221      43.804  17.478  76.063  1.00 47.45      AAAA C
ATOM   2116  SG  CYS   221      45.494  16.935  76.538  1.00 47.06      AAAA S
ATOM   2117  N   ARG   222      40.503  17.133  76.396  1.00 51.47      AAAA N
ATOM   2119  CA  ARG   222      39.281  17.906  76.338  1.00 51.86      AAAA C
ATOM   2120  CB  ARG   222      38.647  18.074  77.712  1.00 54.53      AAAA C
ATOM   2121  CG  ARG   222      37.314  18.687  77.854  1.00 45.56      AAAA C
ATOM   2122  CD  ARG   222      36.538  18.338  79.087  1.00 54.45      AAAA C
ATOM   2123  NE  ARG   222      36.272  16.947  79.269  1.00 65.53      AAAA N
ATOM   2125  CZ  ARG   222      35.534  16.080  78.617  1.00 67.60      AAAA C
ATOM   2126  NH1 ARG   222      34.925  16.599  77.533  1.00 70.26      AAAA N
ATOM   2129  NH2 ARG   222      35.342  14.780  78.901  1.00 54.11      AAAA N
ATOM   2132  C   ARG   222      39.562  19.286  75.740  1.00 50.66      AAAA C
ATOM   2133  O   ARG   222      38.737  19.845  75.009  1.00 58.34      AAAA O
ATOM   2134  N   HIS   223      40.556  19.981  76.190  1.00 45.65      AAAA N
ATOM   2136  CA  HIS   223      40.988  21.291  75.921  1.00 46.93      AAAA C
ATOM   2137  CB  HIS   223      41.057  22.251  77.011  1.00 49.51      AAAA C
ATOM   2138  CG  HIS   223      39.710  22.344  77.647  1.00 58.83      AAAA C
ATOM   2139  CD2 HIS   223      38.820  23.360  77.556  1.00 61.08      AAAA C
ATOM   2140  ND1 HIS   223      39.082  21.388  78.425  1.00 63.28      AAAA N
ATOM   2142  CE1 HIS   223      37.881  21.815  78.759  1.00 58.01      AAAA C
ATOM   2143  NE2 HIS   223      37.681  23.010  78.232  1.00 48.56      AAAA N
ATOM   2145  C   HIS   223      42.363  21.260  75.122  1.00 50.78      AAAA C
ATOM   2146  O   HIS   223      42.506  20.753  74.003  1.00 47.43      AAAA O
ATOM   2147  N   TYR   224      43.359  21.847  75.769  1.00 49.20      AAAA N
ATOM   2149  CA  TYR   224      44.712  21.992  75.259  1.00 48.17      AAAA C
ATOM   2150  CB  TYR   224      45.144  23.430  75.426  1.00 44.07      AAAA C
ATOM   2151  CG  TYR   224      44.318  24.234  74.417  1.00 51.77      AAAA C
ATOM   2152  CD1 TYR   224      43.193  24.869  74.904  1.00 48.94      AAAA C
ATOM   2153  CE1 TYR   224      42.401  25.633  74.089  1.00 48.41      AAAA C
ATOM   2154  CD2 TYR   224      44.623  24.358  73.065  1.00 54.82      AAAA C
ATOM   2155  CE2 TYR   224      43.847  25.131  72.233  1.00 56.09      AAAA C
ATOM   2156  CZ  TYR   224      42.739  25.745  72.766  1.00 54.23      AAAA C
ATOM   2157  OH  TYR   224      41.915  26.522  72.017  1.00 61.70      AAAA O
ATOM   2159  C   TYR   224      45.725  21.095  75.892  1.00 48.19      AAAA C
ATOM   2160  O   TYR   224      45.776  20.913  77.111  1.00 55.75      AAAA O
ATOM   2161  N   TYR   225      46.584  20.514  75.077  1.00 48.79      AAAA N
ATOM   2163  CA  TYR   225      47.655  19.653  75.555  1.00 43.02      AAAA C
ATOM   2164  CB  TYR   225      48.020  18.639  74.548  1.00 42.32      AAAA C
ATOM   2165  CG  TYR   225      49.286  17.926  74.954  1.00 46.95      AAAA C
ATOM   2166  CD1 TYR   225      49.299  16.858  75.817  1.00 43.57      AAAA C
ATOM   2167  CE1 TYR   225      50.450  16.221  76.173  1.00 47.26      AAAA C
ATOM   2168  CD2 TYR   225      50.487  18.407  74.421  1.00 52.82      AAAA C
ATOM   2169  CE2 TYR   225      51.656  17.791  74.781  1.00 53.94      AAAA C
ATOM   2170  CZ  TYR   225      51.639  16.707  75.644  1.00 52.31      AAAA C
ATOM   2171  OH  TYR   225      52.886  16.196  75.905  1.00 50.71      AAAA O
ATOM   2173  C   TYR   225      48.872  20.507  75.793  1.00 47.13      AAAA C
ATOM   2174  O   TYR   225      49.080  21.514  75.150  1.00 53.97      AAAA O
ATOM   2175  N   TYR   226      49.634  20.253  76.821  1.00 56.84      AAAA N
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ATOM   2177  CA  TYR   226      50.814  21.001  77.172  1.00 56.83      AAAA C
ATOM   2178  CB  TYR   226      50.455  22.343  77.785  1.00 59.51      AAAA C
ATOM   2179  CG  TYR   226      51.741  23.126  77.941  1.00 65.45      AAAA C
ATOM   2180  CD1 TYR   226      52.121  23.557  79.197  1.00 69.12      AAAA C
ATOM   2181  CE1 TYR   226      53.289  24.275  79.400  1.00 70.77      AAAA C
ATOM   2182  CD2 TYR   226      52.580  23.409  76.864  1.00 69.38      AAAA C
ATOM   2183  CE2 TYR   226      53.758  24.118  77.020  1.00 70.94      AAAA C
ATOM   2184  CZ  TYR   226      54.099  24.549  78.301  1.00 72.96      AAAA C
ATOM   2185  OH  TYR   226      55.267  25.254  78.435  1.00 70.84      AAAA O
ATOM   2187  C   TYR   226      51.784  20.356  78.165  1.00 57.55      AAAA C
ATOM   2188  O   TYR   226      51.492  20.133  79.350  1.00 56.90      AAAA O
ATOM   2189  N   ALA   227      52.978  20.080  77.642  1.00 53.82      AAAA N
ATOM   2191  CA  ALA   227      54.061  19.557  78.440  1.00 51.82      AAAA C
ATOM   2192  CB  ALA   227      54.528  20.620  79.428  1.00 55.81      AAAA C
ATOM   2193  C   ALA   227      53.600  18.309  79.170  1.00 53.56      AAAA C
ATOM   2194  O   ALA   227      53.663  18.218  80.413  1.00 49.63      AAAA O
ATOM   2195  N   GLY   228      53.076  17.360  78.393  1.00 50.68      AAAA N
ATOM   2197  CA  GLY   228      52.585  16.135  79.028  1.00 49.02      AAAA C
ATOM   2198  C   GLY   228      51.312  16.330  79.861  1.00 51.61      AAAA C
ATOM   2199  O   GLY   228      51.028  15.538  80.776  1.00 51.10      AAAA O
ATOM   2200  N   VAL   229      50.643  17.495  79.791  1.00 47.09      AAAA N
ATOM   2202  CA  VAL   229      49.489  17.671  80.635  1.00 51.11      AAAA C
ATOM   2203  CB  VAL   229      49.908  18.610  81.774  1.00 56.52      AAAA C
ATOM   2204  CG1 VAL   229      48.627  18.896  82.566  1.00 38.39      AAAA C
ATOM   2205  CG2 VAL   229      51.002  18.035  82.682  1.00 50.16      AAAA C
ATOM   2206  C   VAL   229      48.255  18.173  79.873  1.00 51.37      AAAA C
ATOM   2207  O   VAL   229      48.344  19.279  79.309  1.00 53.71      AAAA O
ATOM   2208  N   CYS   230      47.100  17.518  80.036  1.00 42.21      AAAA N
ATOM   2210  CA  CYS   230      45.881  18.117  79.471  1.00 40.32      AAAA C
ATOM   2211  C   CYS   230      45.456  19.350  80.228  1.00 38.42      AAAA C
ATOM   2212  O   CYS   230      44.964  19.248  81.321  1.00 41.62      AAAA O
ATOM   2213  CB  CYS   230      44.746  17.132  79.370  1.00 31.54      AAAA C
ATOM   2214  SG  CYS   230      45.149  15.753  78.266  1.00 43.61      AAAA S
ATOM   2215  N   VAL   231      45.637  20.534  79.731  1.00 39.83      AAAA N
ATOM   2217  CA  VAL   231      45.445  21.769  80.462  1.00 46.57      AAAA C
ATOM   2218  CB  VAL   231      46.618  22.736  80.088  1.00 50.99      AAAA C
ATOM   2219  CG1 VAL   231      46.798  23.878  81.053  1.00 50.41      AAAA C
ATOM   2220  CG2 VAL   231      47.838  21.913  80.506  1.00 44.95      AAAA C
ATOM   2221  C   VAL   231      44.111  22.321  80.057  1.00 52.59      AAAA C
ATOM   2222  O   VAL   231      43.599  22.183  78.936  1.00 55.30      AAAA O
ATOM   2223  N   PRO   232      43.482  23.105  80.913  1.00 54.28      AAAA N
ATOM   2224  CD  PRO   232      43.830  23.385  82.320  1.00 54.25      AAAA C
ATOM   2225  CA  PRO   232      42.153  23.625  80.575  1.00 54.39      AAAA C
ATOM   2226  CB  PRO   232      41.537  23.877  81.928  1.00 53.73      AAAA C
ATOM   2227  CG  PRO   232      42.683  24.287  82.765  1.00 55.00      AAAA C
ATOM   2228  C   PRO   232      42.361  24.913  79.795  1.00 56.37      AAAA C
ATOM   2229  O   PRO   232      41.498  25.482  79.137  1.00 55.79      AAAA O
ATOM   2230  N   ALA   233      43.615  25.400  79.901  1.00 54.76      AAAA N
ATOM   2232  CA  ALA   233      43.998  26.569  79.124  1.00 49.93      AAAA C
ATOM   2233  CB  ALA   233      43.440  27.807  79.746  1.00 35.43      AAAA C
ATOM   2234  C   ALA   233      45.502  26.662  78.974  1.00 49.79      AAAA C
ATOM   2235  O   ALA   233      46.195  25.879  79.616  1.00 51.41      AAAA O
ATOM   2236  N   CYS   234      45.984  27.508  78.072  1.00 45.07      AAAA N
ATOM   2238  CA  CYS   234      47.430  27.518  77.907  1.00 48.63      AAAA C
ATOM   2239  C   CYS   234      48.001  28.340  79.076  1.00 50.93      AAAA C
ATOM   2240  O   CYS   234      47.650  29.513  79.250  1.00 47.57      AAAA O
ATOM   2241  CB  CYS   234      47.816  28.034  76.511  1.00 43.10      AAAA C
ATOM   2242  SG  CYS   234      47.608  26.789  75.226  1.00 43.04      AAAA S
ATOM   2243  N   PRO   235      49.127  27.853  79.599  1.00 49.55      AAAA N
ATOM   2244  CD  PRO   235      49.692  26.557  79.207  1.00 48.75      AAAA C
ATOM   2245  CA  PRO   235      49.911  28.569  80.599  1.00 51.69      AAAA C
ATOM   2246  CB  PRO   235      50.984  27.581  80.975  1.00 50.80      AAAA C
ATOM   2247  CG  PRO   235      50.912  26.417  80.077  1.00 50.06      AAAA C
ATOM   2248  C   PRO   235      50.487  29.852  80.050  1.00 57.11      AAAA C
ATOM   2249  O   PRO   235      50.848  29.957  78.870  1.00 59.60      AAAA O
ATOM   2250  N   PRO   236      50.676  30.875  80.887  1.00 59.85      AAAA N
ATOM   2251  CD  PRO   236      50.405  30.822  82.363  1.00 55.85      AAAA C
ATOM   2252  CA  PRO   236      51.323  32.143  80.493  1.00 52.27      AAAA C
ATOM   2253  CB  PRO   236      51.695  32.814  81.826  1.00 53.62      AAAA C
ATOM   2254  CG  PRO   236      50.652  32.277  82.754  1.00 56.73      AAAA C
ATOM   2255  C   PRO   236      52.545  31.886  79.671  1.00 44.21      AAAA C
ATOM   2256  O   PRO   236      53.218  30.892  79.928  1.00 43.40      AAAA O
ATOM   2257  N   ASN   237      52.837  32.757  78.716  1.00 46.54      AAAA N
ATOM   2259  CA  ASN   237      53.895  32.623  77.716  1.00 45.94      AAAA C
ATOM   2260  CB  ASN   237      55.258  32.653  78.456  1.00 58.65      AAAA C
ATOM   2261  CG  ASN   237      55.357  33.855  79.371  1.00 58.51      AAAA C
ATOM   2262  OD1 ASN   237      56.044  33.783  80.379  1.00 72.25      AAAA O
ATOM   2263  ND2 ASN   237      54.631  34.910  79.051  1.00 62.99      AAAA N
ATOM   2266  C   ASN   237      53.897  31.425  76.788  1.00 46.87      AAAA C
ATOM   2267  O   ASN   237      54.962  30.935  76.326  1.00 54.50      AAAA O
ATOM   2268  N   THR   238      52.817  30.657  76.692  1.00 42.91      AAAA N
ATOM   2270  CA  THR   238      52.617  29.567  75.780  1.00 40.20      AAAA C
ATOM   2271  CB  THR   238      52.461  28.248  76.466  1.00 42.62      AAAA C
ATOM   2272  OG1 THR   238      51.227  28.343  77.237  1.00 50.88      AAAA O
ATOM   2274  CG2 THR   238      53.552  27.986  77.424  1.00 34.84      AAAA C
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ATOM   2275  C   THR   238      51.279  29.875  75.078  1.00 42.59      AAAA C
ATOM   2276  O   THR   238      50.669  30.864  75.509  1.00 42.51      AAAA O
ATOM   2277  N   TYR   239      51.051  29.488  73.832  1.00 42.62      AAAA N
ATOM   2279  CA  TYR   239      49.949  29.959  73.024  1.00 41.87      AAAA C
ATOM   2280  CB  TYR   239      50.457  30.907  71.931  1.00 44.86      AAAA C
ATOM   2281  CG  TYR   239      51.099  32.125  72.564  1.00 42.05      AAAA C
ATOM   2282  CD1 TYR   239      52.467  32.086  72.815  1.00 39.41      AAAA C
ATOM   2283  CE1 TYR   239      53.092  33.152  73.415  1.00 43.27      AAAA C
ATOM   2284  CD2 TYR   239      50.376  33.230  72.923  1.00 44.15      AAAA C
ATOM   2285  CE2 TYR   239      50.972  34.310  73.536  1.00 46.22      AAAA C
ATOM   2286  CZ  TYR   239      52.339  34.243  73.779  1.00 50.49      AAAA C
ATOM   2287  OH  TYR   239      53.013  35.289  74.387  1.00 55.47      AAAA O
ATOM   2289  C   TYR   239      49.232  28.813  72.315  1.00 45.54      AAAA C
ATOM   2290  O   TYR   239      49.922  27.810  72.021  1.00 46.66      AAAA O
ATOM   2291  N   ARG   240      47.895  28.990  72.126  1.00 40.62      AAAA N
ATOM   2293  CA  ARG   240      47.177  27.892  71.426  1.00 38.78      AAAA C
ATOM   2294  CB  ARG   240      45.675  28.127  71.452  1.00 39.77      AAAA C
ATOM   2295  CG  ARG   240      45.116  28.944  72.588  1.00 43.37      AAAA C
ATOM   2296  CD  ARG   240      43.573  28.957  72.683  1.00 38.60      AAAA C
ATOM   2297  NE  ARG   240      43.114  29.683  71.455  1.00 53.98      AAAA N
ATOM   2299  CZ  ARG   240      43.123  31.015  71.530  1.00 48.07      AAAA C
ATOM   2300  NH1 ARG   240      43.513  31.562  72.668  1.00 47.65      AAAA N
ATOM   2303  NH2 ARG   240      42.788  31.778  70.533  1.00 51.03      AAAA N
ATOM   2306  C   ARG   240      47.627  27.737  69.979  1.00 31.72      AAAA C
ATOM   2307  O   ARG   240      47.937  28.730  69.302  1.00 32.37      AAAA O
ATOM   2308  N   PHE   241      47.779  26.542  69.549  1.00 27.95      AAAA N
ATOM   2310  CA  PHE   241      48.182  26.269  68.183  1.00 30.41      AAAA C
ATOM   2311  CB  PHE   241      49.678  25.940  68.151  1.00 34.83      AAAA C
ATOM   2312  CG  PHE   241      50.235  25.653  66.773  1.00 26.84      AAAA C
ATOM   2313  CD1 PHE   241      50.165  26.567  65.753  1.00 25.31      AAAA C
ATOM   2314  CD2 PHE   241      50.785  24.417  66.573  1.00 27.38      AAAA C
ATOM   2315  CE1 PHE   241      50.676  26.232  64.509  1.00 37.24      AAAA C
ATOM   2316  CE2 PHE   241      51.294  24.101  65.320  1.00 38.45      AAAA C
ATOM   2317  CZ  PHE   241      51.281  25.010  64.281  1.00 21.17      AAAA C
ATOM   2318  C   PHE   241      47.382  25.089  67.621  1.00 35.77      AAAA C
ATOM   2319  O   PHE   241      47.543  24.013  68.186  1.00 36.77      AAAA O
ATOM   2320  N   GLU   242      46.738  25.301  66.468  1.00 32.30      AAAA N
ATOM   2322  CA  GLU   242      45.964  24.269  65.805  1.00 35.43      AAAA C
ATOM   2323  CB  GLU   242      46.953  23.144  65.472  1.00 37.98      AAAA C
ATOM   2324  CG  GLU   242      47.867  23.415  64.314  1.00 38.63      AAAA C
ATOM   2325  CD  GLU   242      47.207  23.965  63.075  1.00 39.27      AAAA C
ATOM   2326  OE1 GLU   242      46.380  23.205  62.517  1.00 42.79      AAAA O
ATOM   2327  OE2 GLU   242      47.354  25.109  62.626  1.00 36.36      AAAA O
ATOM   2328  C   GLU   242      44.752  23.771  66.600  1.00 34.36      AAAA C
ATOM   2329  O   GLU   242      44.390  22.611  66.511  1.00 28.53      AAAA O
ATOM   2330  N   GLY   243      44.135  24.589  67.449  1.00 36.94      AAAA N
ATOM   2332  CA  GLY   243      43.048  24.154  68.303  1.00 34.57      AAAA C
ATOM   2333  C   GLY   243      43.428  23.107  69.319  1.00 37.76      AAAA C
ATOM   2334  O   GLY   243      42.474  22.473  69.746  1.00 43.00      AAAA O
ATOM   2335  N   TRP   244      44.637  22.636  69.611  1.00 39.53      AAAA N
ATOM   2337  CA  TRP   244      44.797  21.536  70.566  1.00 40.85      AAAA C
ATOM   2338  CB  TRP   244      44.774  20.271  69.764  1.00 26.76      AAAA C
ATOM   2339  CG  TRP   244      46.012  19.885  69.028  1.00 43.19      AAAA C
ATOM   2340  CD2 TRP   244      47.019  18.983  69.498  1.00 39.55      AAAA C
ATOM   2341  CE2 TRP   244      47.998  18.906  68.489  1.00 36.50      AAAA C
ATOM   2342  CE3 TRP   244      47.186  18.254  70.692  1.00 32.18      AAAA C
ATOM   2343  CD1 TRP   244      46.424  20.308  67.779  1.00 43.37      AAAA C
ATOM   2344  NE1 TRP   244      47.595  19.727  67.469  1.00 38.89      AAAA N
ATOM   2346  CZ2 TRP   244      49.150  18.128  68.620  1.00 39.01      AAAA C
ATOM   2347  CZ3 TRP   244      48.336  17.478  70.815  1.00 43.98      AAAA C
ATOM   2348  CH2 TRP   244      49.322  17.425  69.784  1.00 42.50      AAAA C
ATOM   2349  C   TRP   244      45.998  21.517  71.509  1.00 42.98      AAAA C
ATOM   2350  O   TRP   244      46.253  20.501  72.146  1.00 42.70      AAAA O
ATOM   2351  N   ARG   245      46.888  22.485  71.435  1.00 44.16      AAAA N
ATOM   2353  CA  ARG   245      48.168  22.472  72.095  1.00 46.47      AAAA C
ATOM   2354  CB  ARG   245      49.203  21.602  71.367  1.00 47.30      AAAA C
ATOM   2355  CG  ARG   245      49.885  22.309  70.203  1.00 48.97      AAAA C
ATOM   2356  CD  ARG   245      51.129  21.552  69.819  1.00 39.28      AAAA C
ATOM   2357  NE  ARG   245      51.586  21.665  68.444  1.00 50.86      AAAA N
ATOM   2359  CZ  ARG   245      52.629  21.044  67.895  1.00 46.73      AAAA C
ATOM   2360  NH1 ARG   245      53.344  20.236  68.653  1.00 50.15      AAAA N
ATOM   2363  NH2 ARG   245      53.072  21.126  66.638  1.00 41.69      AAAA N
ATOM   2366  C   ARG   245      48.771  23.863  72.271  1.00 46.01      AAAA C
ATOM   2367  O   ARG   245      48.394  24.793  71.541  1.00 47.44      AAAA O
ATOM   2368  N   CYS   246      49.625  23.881  73.317  1.00 42.08      AAAA N
ATOM   2370  CA  CYS   246      50.246  25.199  73.628  1.00 43.48      AAAA C
ATOM   2371  C   CYS   246      51.695  25.217  73.183  1.00 43.38      AAAA C
ATOM   2372  O   CYS   246      52.476  24.239  73.320  1.00 42.51      AAAA O
ATOM   2373  CB  CYS   246      50.102  25.392  75.138  1.00 48.91      AAAA C
ATOM   2374  SG  CYS   246      48.386  25.049  75.797  1.00 43.68      AAAA S
ATOM   2375  N   VAL   247      52.121  26.288  72.564  1.00 41.21      AAAA N
ATOM   2377  CA  VAL   247      53.417  26.468  71.982  1.00 36.51      AAAA C
ATOM   2378  CB  VAL   247      53.568  26.357  70.444  1.00 36.87      AAAA C
ATOM   2379  CG1 VAL   247      53.089  24.988  70.024  1.00 32.71      AAAA C
ATOM   2380  CG2 VAL   247      53.129  27.602  69.729  1.00 28.20      AAAA C
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ATOM   2381  C   VAL   247      53.969  27.812  72.373  1.00 39.37      AAAA C
ATOM   2382  O   VAL   247      53.230  28.770  72.540  1.00 38.80      AAAA O
ATOM   2383  N   ASP   248      55.291  27.820  72.711  1.00 45.21      AAAA N
ATOM   2385  CA  ASP   248      55.895  29.115  73.098  1.00 40.19      AAAA C
ATOM   2386  CB  ASP   248      57.091  28.946  73.953  1.00 42.63      AAAA C
ATOM   2387  CG  ASP   248      58.126  27.997  73.394  1.00 58.81      AAAA C
ATOM   2388  OD1 ASP   248      59.067  27.795  74.187  1.00 53.06      AAAA O
ATOM   2389  OD2 ASP   248      58.167  27.395  72.313  1.00 69.51      AAAA O
ATOM   2390  C   ASP   248      56.315  29.883  71.839  1.00 36.99      AAAA C
ATOM   2391  O   ASP   248      56.292  29.288  70.772  1.00 39.70      AAAA O
ATOM   2392  N   ARG   249      56.545  31.163  71.918  1.00 30.72      AAAA N
ATOM   2394  CA  ARG   249      56.950  32.057  70.906  1.00 36.17      AAAA C
ATOM   2395  CB  ARG   249      57.223  33.485  71.491  1.00 21.29      AAAA C
ATOM   2396  CG  ARG   249      57.594  34.424  70.326  1.00 24.96      AAAA C
ATOM   2397  CD  ARG   249      57.814  35.811  70.843  1.00 21.23      AAAA C
ATOM   2398  NE  ARG   249      56.658  36.150  71.689  1.00 39.75      AAAA N
ATOM   2400  CZ  ARG   249      55.632  36.823  71.101  1.00 39.35      AAAA C
ATOM   2401  NH1 ARG   249      55.642  37.118  69.801  1.00 25.41      AAAA N
ATOM   2404  NH2 ARG   249      54.641  37.118  71.946  1.00 44.04      AAAA N
ATOM   2407  C   ARG   249      58.134  31.685  70.010  1.00 40.63      AAAA C
ATOM   2408  O   ARG   249      58.086  31.923  68.797  1.00 44.79      AAAA O
ATOM   2409  N   ASP   250      59.149  30.974  70.468  1.00 41.87      AAAA N
ATOM   2411  CA  ASP   250      60.287  30.739  69.606  1.00 46.90      AAAA C
ATOM   2412  CB  ASP   250      61.740  30.726  70.154  1.00 53.11      AAAA C
ATOM   2413  CG  ASP   250      62.421  32.122  70.081  1.00 71.49      AAAA C
ATOM   2414  OD1 ASP   250      63.124  32.682  69.176  1.00 58.53      AAAA O
ATOM   2415  OD2 ASP   250      62.272  32.928  71.071  1.00 70.30      AAAA O
ATOM   2416  C   ASP   250      59.881  29.536  68.771  1.00 41.22      AAAA C
ATOM   2417  O   ASP   250      60.291  29.443  67.616  1.00 39.06      AAAA O
ATOM   2418  N   PHE   251      59.116  28.609  69.299  1.00 36.13      AAAA N
ATOM   2420  CA  PHE   251      58.457  27.601  68.489  1.00 34.88      AAAA C
ATOM   2421  CB  PHE   251      57.468  26.746  69.256  1.00 29.82      AAAA C
ATOM   2422  CG  PHE   251      56.701  25.801  68.385  1.00 41.50      AAAA C
ATOM   2423  CD1 PHE   251      57.101  24.479  68.263  1.00 30.66      AAAA C
ATOM   2424  CD2 PHE   251      55.559  26.213  67.686  1.00 37.78      AAAA C
ATOM   2425  CE1 PHE   251      56.414  23.597  67.424  1.00 29.30      AAAA C
ATOM   2426  CE2 PHE   251      54.847  25.372  66.856  1.00 36.09      AAAA C
ATOM   2427  CZ  PHE   251      55.294  24.070  66.715  1.00 36.21      AAAA C
ATOM   2428  C   PHE   251      57.624  28.290  67.338  1.00 39.28      AAAA C
ATOM   2429  O   PHE   251      57.811  28.010  66.144  1.00 30.27      AAAA O
ATOM   2430  N   CYS   252      56.734  29.225  67.713  1.00 35.13      AAAA N
ATOM   2432  CA  CYS   252      55.895  29.870  66.728  1.00 38.80      AAAA C
ATOM   2433  C   CYS   252      56.827  30.598  65.747  1.00 44.73      AAAA C
ATOM   2434  O   CYS   252      56.552  30.534  64.536  1.00 43.20      AAAA O
ATOM   2435  CB  CYS   252      54.903  30.778  67.379  1.00 35.65      AAAA C
ATOM   2436  SG  CYS   252      53.562  31.544  66.459  1.00 39.03      AAAA S
ATOM   2437  N   ALA   253      57.872  31.256  66.285  1.00 41.53      AAAA N
ATOM   2439  CA  ALA   253      58.687  32.071  65.415  1.00 40.39      AAAA C
ATOM   2440  CB  ALA   253      59.529  33.088  66.172  1.00 36.07      AAAA C
ATOM   2441  C   ALA   253      59.551  31.167  64.539  1.00 42.88      AAAA C
ATOM   2442  O   ALA   253      60.147  31.735  63.640  1.00 47.42      AAAA O
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ATOM   2446  CB  ASN   254      61.667  28.497  64.847  1.00 48.09      AAAA C
ATOM   2447  CG  ASN   254      62.696  29.635  65.031  1.00 49.54      AAAA C
ATOM   2448  OD1 ASN   254      63.468  29.840  64.081  1.00 61.38      AAAA O
ATOM   2449  ND2 ASN   254      62.607  30.321  66.144  1.00 48.38      AAAA N
ATOM   2452  C   ASN   254      59.907  27.959  63.135  1.00 53.72      AAAA C
ATOM   2453  O   ASN   254      60.552  26.965  62.804  1.00 51.19      AAAA O
ATOM   2454  N   ILE   255      58.612  28.136  62.766  1.00 57.77      AAAA N
ATOM   2456  CA  ILE   255      57.828  27.107  62.134  1.00 53.28      AAAA C
ATOM   2457  CB  ILE   255      56.329  27.322  62.304  1.00 50.41      AAAA C
ATOM   2458  CG2 ILE   255      55.477  26.595  61.246  1.00 51.95      AAAA C
ATOM   2459  CG1 ILE   255      55.778  26.675  63.553  1.00 40.59      AAAA C
ATOM   2460  CD1 ILE   255      54.479  27.317  64.006  1.00 38.97      AAAA C
ATOM   2461  C   ILE   255      58.127  26.886  60.651  1.00 52.62      AAAA C
ATOM   2462  O   ILE   255      58.196  25.709  60.252  1.00 53.96      AAAA O
ATOM   2463  N   LEU   256      58.290  27.960  59.918  1.00 49.96      AAAA N
ATOM   2465  CA  LEU   256      58.680  27.764  58.516  1.00 63.68      AAAA C
ATOM   2466  CB  LEU   256      58.175  29.012  57.799  1.00 56.80      AAAA C
ATOM   2467  CG  LEU   256      56.671  29.196  57.864  1.00 59.11      AAAA C
ATOM   2468  CD1 LEU   256      56.310  30.654  57.645  1.00 43.31      AAAA C
ATOM   2469  CD2 LEU   256      55.965  28.222  56.928  1.00 55.88      AAAA C
ATOM   2470  C   LEU   256      60.193  27.622  58.355  1.00 66.23      AAAA C
ATOM   2471  O   LEU   256      60.691  27.511  57.245  1.00 70.29      AAAA O
ATOM   2472  N   SER   257      60.942  27.559  59.430  1.00 64.61      AAAA N
ATOM   2474  CA  SER   257      62.352  27.529  59.534  1.00 69.23      AAAA C
ATOM   2475  CB  SER   257      62.924  27.318  60.955  1.00 62.45      AAAA C
ATOM   2476  OG  SER   257      63.381  25.980  61.074  1.00 56.18      AAAA O
ATOM   2478  C   SER   257      62.973  26.497  58.610  1.00 70.77      AAAA C
ATOM   2479  O   SER   257      64.127  26.731  58.246  1.00 72.50      AAAA O
ATOM   2480  N   ALA   258      62.322  25.389  58.329  1.00 74.61      AAAA N
ATOM   2482  CA  ALA   258      62.933  24.488  57.343  1.00 76.34      AAAA C
ATOM   2483  CB  ALA   258      62.570  23.039  57.584  1.00 80.82      AAAA C
ATOM   2484  C   ALA   258      62.663  24.964  55.921  1.00 78.21      AAAA C
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ATOM   2485  O   ALA   258      62.880  24.139  55.029  1.00 79.60      AAAA O
ATOM   2486  N   GLU   259      62.069  26.109  55.651  1.00 79.05      AAAA N
ATOM   2488  CA  GLU   259      61.742  26.621  54.342  1.00 83.84      AAAA C
ATOM   2489  CB  GLU   259      60.226  26.457  54.135  1.00 86.99      AAAA C
ATOM   2490  CG  GLU   259      59.687  25.049  54.314  1.00 89.38      AAAA C
ATOM   2491  CD  GLU   259      58.364  25.032  55.057  1.00 97.77      AAAA C
ATOM   2492  OE1 GLU   259      58.080  24.088  55.838  1.00101.45      AAAA O
ATOM   2493  OE2 GLU   259      57.598  26.002  54.837  1.00 94.58      AAAA O
ATOM   2494  C   GLU   259      62.117  28.078  54.083  1.00 85.43      AAAA C
ATOM   2495  O   GLU   259      62.059  29.009  54.903  1.00 88.01      AAAA O
ATOM   2496  N   SER   260      62.298  28.338  52.799  1.00 84.66      AAAA N
ATOM   2498  CA  SER   260      62.725  29.625  52.254  1.00 84.03      AAAA C
ATOM   2499  CB  SER   260      63.753  29.269  51.173  1.00 87.24      AAAA C
ATOM   2500  OG  SER   260      63.306  29.419  49.835  1.00 93.65      AAAA O
ATOM   2502  C   SER   260      61.558  30.466  51.789  1.00 80.84      AAAA C
ATOM   2503  O   SER   260      61.496  30.889  50.635  1.00 81.31      AAAA O
ATOM   2504  N   SER   261      60.617  30.785  52.685  1.00 78.56      AAAA N
ATOM   2506  CA  SER   261      59.423  31.540  52.308  1.00 72.13      AAAA C
ATOM   2507  CB  SER   261      58.179  31.297  53.170  1.00 67.30      AAAA C
ATOM   2508  OG  SER   261      57.436  30.334  52.451  1.00 74.74      AAAA O
ATOM   2510  C   SER   261      59.683  33.032  52.318  1.00 66.90      AAAA C
ATOM   2511  O   SER   261      60.048  33.588  53.334  1.00 63.24      AAAA O
ATOM   2512  N   ASP   262      59.364  33.659  51.204  1.00 65.30      AAAA N
ATOM   2514  CA  ASP   262      59.358  35.071  50.915  1.00 58.55      AAAA C
ATOM   2515  CB  ASP   262      59.268  35.285  49.400  1.00 64.85      AAAA C
ATOM   2516  CG  ASP   262      59.389  36.713  48.931  1.00 76.42      AAAA C
ATOM   2517  OD1 ASP   262      59.473  37.708  49.701  1.00 79.81      AAAA O
ATOM   2518  OD2 ASP   262      59.404  36.873  47.671  1.00 80.46      AAAA O
ATOM   2519  C   ASP   262      58.121  35.706  51.529  1.00 56.88      AAAA C
ATOM   2520  O   ASP   262      57.851  36.918  51.510  1.00 52.48      AAAA O
ATOM   2521  N   SER   263      57.259  34.849  52.118  1.00 53.43      AAAA N
ATOM   2523  CA  SER   263      56.047  35.352  52.734  1.00 52.84      AAAA C
ATOM   2524  CB  SER   263      55.020  34.245  52.885  1.00 46.60      AAAA C
ATOM   2525  OG  SER   263      55.149  33.348  51.791  1.00 66.80      AAAA O
ATOM   2527  C   SER   263      56.310  35.965  54.117  1.00 49.52      AAAA C
ATOM   2528  O   SER   263      57.396  35.737  54.709  1.00 42.33      AAAA O
ATOM   2529  N   GLU   264      55.320  36.783  54.540  1.00 38.93      AAAA N
ATOM   2531  CA  GLU   264      55.362  37.222  55.921  1.00 36.70      AAAA C
ATOM   2532  CB  GLU   264      54.359  38.337  56.208  1.00 43.71      AAAA C
ATOM   2533  CG  GLU   264      54.575  39.482  55.218  1.00 37.74      AAAA C
ATOM   2534  CD  GLU   264      55.374  40.632  55.793  1.00 34.36      AAAA C
ATOM   2535  OE1 GLU   264      55.493  40.600  57.034  1.00 41.55      AAAA O
ATOM   2536  OE2 GLU   264      55.832  41.576  55.146  1.00 39.60      AAAA O
ATOM   2537  C   GLU   264      55.098  36.056  56.827  1.00 35.84      AAAA C
ATOM   2538  O   GLU   264      54.368  35.151  56.355  1.00 39.60      AAAA O
ATOM   2539  N   GLY   265      55.801  35.938  57.962  1.00 35.64      AAAA N
ATOM   2541  CA  GLY   265      55.671  34.690  58.727  1.00 40.30      AAAA C
ATOM   2542  C   GLY   265      54.622  34.716  59.829  1.00 39.51      AAAA C
ATOM   2543  O   GLY   265      53.951  35.699  60.135  1.00 37.20      AAAA O
ATOM   2544  N   PHE   266      54.537  33.569  60.516  1.00 35.75      AAAA N
ATOM   2546  CA  PHE   266      53.637  33.434  61.625  1.00 33.70      AAAA C
ATOM   2547  CB  PHE   266      53.924  32.155  62.386  1.00 28.20      AAAA C
ATOM   2548  CG  PHE   266      53.356  30.958  61.671  1.00 37.07      AAAA C
ATOM   2549  CD1 PHE   266      53.760  30.618  60.377  1.00 34.72      AAAA C
ATOM   2550  CD2 PHE   266      52.383  30.185  62.313  1.00 25.65      AAAA C
ATOM   2551  CE1 PHE   266      53.225  29.506  59.760  1.00 37.72      AAAA C
ATOM   2552  CE2 PHE   266      51.879  29.094  61.672  1.00 24.63      AAAA C
ATOM   2553  CZ  PHE   266      52.260  28.708  60.402  1.00 23.58      AAAA C
ATOM   2554  C   PHE   266      53.571  34.570  62.608  1.00 35.82      AAAA C
ATOM   2555  O   PHE   266      54.446  35.372  62.879  1.00 39.23      AAAA O
ATOM   2556  N   VAL   267      52.360  34.763  63.161  1.00 37.10      AAAA N
ATOM   2558  CA  VAL   267      52.118  35.812  64.113  1.00 36.09      AAAA C
ATOM   2559  CB  VAL   267      51.315  36.974  63.567  1.00 39.01      AAAA C
ATOM   2560  CG1 VAL   267      51.626  37.601  62.230  1.00 31.10      AAAA C
ATOM   2561  CG2 VAL   267      49.890  36.400  63.570  1.00 36.88      AAAA C
ATOM   2562  C   VAL   267      51.506  35.260  65.400  1.00 33.55      AAAA C
ATOM   2563  O   VAL   267      51.202  34.098  65.515  1.00 32.41      AAAA O
ATOM   2564  N   ILE   268      51.539  36.088  66.477  1.00 35.88      AAAA N
ATOM   2566  CA  ILE   268      50.867  35.573  67.681  1.00 39.79      AAAA C
ATOM   2567  CB  ILE   268      51.791  35.232  68.849  1.00 31.17      AAAA C
ATOM   2568  CG2 ILE   268      50.922  35.253  70.150  1.00 32.66      AAAA C
ATOM   2569  CG1 ILE   268      52.403  33.866  68.724  1.00 23.56      AAAA C
ATOM   2570  CD1 ILE   268      53.421  33.546  69.806  1.00 25.93      AAAA C
ATOM   2571  C   ILE   268      49.806  36.608  68.060  1.00 42.44      AAAA C
ATOM   2572  O   ILE   268      50.116  37.767  68.327  1.00 39.99      AAAA O
ATOM   2573  N   HIS   269      48.528  36.292  67.864  1.00 44.26      AAAA N
ATOM   2575  CA  HIS   269      47.491  37.320  68.173  1.00 44.28      AAAA C
ATOM   2576  CB  HIS   269      46.885  37.876  66.901  1.00 45.48      AAAA C
ATOM   2577  CG  HIS   269      45.915  38.986  67.079  1.00 54.33      AAAA C
ATOM   2578  CD2 HIS   269      44.551  39.014  67.096  1.00 46.61      AAAA C
ATOM   2579  ND1 HIS   269      46.356  40.280  67.307  1.00 51.86      AAAA N
ATOM   2581  CE1 HIS   269      45.282  41.057  67.437  1.00 55.17      AAAA C
ATOM   2582  NE2 HIS   269      44.175  40.324  67.309  1.00 46.97      AAAA N
ATOM   2584  C   HIS   269      46.423  36.740  69.074  1.00 45.54      AAAA C
ATOM   2585  O   HIS   269      46.076  35.552  69.027  1.00 42.94      AAAA O
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ATOM   2586  N   ASP   270      45.952  37.526  70.059  1.00 49.82      AAAA N
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ATOM   2589  CB  ASP   270      43.573  37.014  70.338  1.00 63.63      AAAA C
ATOM   2590  CG  ASP   270      42.919  38.393  70.294  1.00 80.82      AAAA C
ATOM   2591  OD1 ASP   270      41.737  38.379  69.835  1.00 90.92      AAAA O
ATOM   2592  OD2 ASP   270      43.407  39.494  70.652  1.00 86.49      AAAA O
ATOM   2593  C   ASP   270      45.226  35.667  71.594  1.00 44.66      AAAA C
ATOM   2594  O   ASP   270      44.357  34.782  71.576  1.00 45.54      AAAA O
ATOM   2595  N   GLY   271      46.477  35.379  71.924  1.00 41.63      AAAA N
ATOM   2597  CA  GLY   271      46.839  34.117  72.506  1.00 37.20      AAAA C
ATOM   2598  C   GLY   271      46.818  32.998  71.537  1.00 39.15      AAAA C
ATOM   2599  O   GLY   271      46.775  31.865  72.039  1.00 46.56      AAAA O
ATOM   2600  N   GLU   272      47.015  33.292  70.251  1.00 41.49      AAAA N
ATOM   2602  CA  GLU   272      47.108  32.092  69.371  1.00 43.56      AAAA C
ATOM   2603  CB  GLU   272      45.752  31.737  68.876  1.00 37.58      AAAA C
ATOM   2604  CG  GLU   272      45.778  30.600  67.839  1.00 45.30      AAAA C
ATOM   2605  CD  GLU   272      44.413  30.528  67.149  1.00 36.92      AAAA C
ATOM   2606  OE1 GLU   272      43.545  31.345  67.533  1.00 48.41      AAAA O
ATOM   2607  OE2 GLU   272      44.223  29.696  66.286  1.00 44.10      AAAA O
ATOM   2608  C   GLU   272      48.211  32.324  68.335  1.00 40.32      AAAA C
ATOM   2609  O   GLU   272      48.445  33.447  67.896  1.00 37.04      AAAA O
ATOM   2610  N   CYS   273      48.942  31.237  68.138  1.00 38.83      AAAA N
ATOM   2612  CA  CYS   273      50.046  31.187  67.188  1.00 40.27      AAAA C
ATOM   2613  C   CYS   273      49.321  30.810  65.883  1.00 42.16      AAAA C
ATOM   2614  O   CYS   273      48.713  29.712  65.831  1.00 40.86      AAAA O
ATOM   2615  CB  CYS   273      51.098  30.148  67.529  1.00 40.21      AAAA C
ATOM   2616  SG  CYS   273      52.337  29.825  66.260  1.00 39.79      AAAA S
ATOM   2617  N   MET   274      49.373  31.749  64.933  1.00 33.70      AAAA N
ATOM   2619  CA  MET   274      48.586  31.351  63.720  1.00 36.68      AAAA C
ATOM   2620  CB  MET   274      47.136  31.861  63.847  1.00 29.11      AAAA C
ATOM   2621  CG  MET   274      46.923  33.379  63.691  1.00 36.51      AAAA C
ATOM   2622  SD  MET   274      45.477  33.921  64.677  1.00 40.00      AAAA S
ATOM   2623  CE  MET   274      45.659  35.658  64.754  1.00 22.47      AAAA C
ATOM   2624  C   MET   274      49.426  31.900  62.608  1.00 39.35      AAAA C
ATOM   2625  O   MET   274      50.167  32.880  62.672  1.00 41.00      AAAA O
ATOM   2626  N   GLN   275      49.378  31.353  61.428  1.00 42.55      AAAA N
ATOM   2628  CA  GLN   275      50.041  31.834  60.232  1.00 37.69      AAAA C
ATOM   2629  CB  GLN   275      49.618  30.765  59.242  1.00 34.01      AAAA C
ATOM   2630  CG  GLN   275      49.329  31.274  57.864  1.00 56.40      AAAA C
ATOM   2631  CD  GLN   275      49.275  30.190  56.812  1.00 66.46      AAAA C
ATOM   2632  OE1 GLN   275      49.941  29.151  56.910  1.00 67.24      AAAA O
ATOM   2633  NE2 GLN   275      48.451  30.436  55.799  1.00 78.29      AAAA N
ATOM   2636  C   GLN   275      49.721  33.195  59.720  1.00 35.41      AAAA C
ATOM   2637  O   GLN   275      50.526  33.831  59.064  1.00 35.95      AAAA O
ATOM   2638  N   GLU   276      48.566  33.754  60.056  1.00 41.70      AAAA N
ATOM   2640  CA  GLU   276      48.222  35.080  59.571  1.00 43.96      AAAA C
ATOM   2641  CB  GLU   276      47.387  34.884  58.245  1.00 42.40      AAAA C
ATOM   2642  CG  GLU   276      47.154  36.269  57.650  1.00 53.84      AAAA C
ATOM   2643  CD  GLU   276      48.359  37.198  57.460  1.00 61.37      AAAA C
ATOM   2644  OE1 GLU   276      49.356  36.595  56.943  1.00 67.32      AAAA O
ATOM   2645  OE2 GLU   276      48.242  38.411  57.811  1.00 45.10      AAAA O
ATOM   2646  C   GLU   276      47.444  35.935  60.540  1.00 39.74      AAAA C
ATOM   2647  O   GLU   276      46.760  35.449  61.444  1.00 45.06      AAAA O
ATOM   2648  N   CYS   277      47.495  37.235  60.500  1.00 38.69      AAAA N
ATOM   2650  CA  CYS   277      46.718  38.089  61.332  1.00 46.11      AAAA C
ATOM   2651  C   CYS   277      45.205  37.938  60.994  1.00 52.70      AAAA C
ATOM   2652  O   CYS   277      44.760  37.511  59.936  1.00 49.43      AAAA O
ATOM   2653  CB  CYS   277      47.039  39.537  61.111  1.00 45.56      AAAA C
ATOM   2654  SG  CYS   277      48.629  40.083  61.645  1.00 52.86      AAAA S
ATOM   2655  N   PRO   278      44.380  38.261  61.993  1.00 54.63      AAAA N
ATOM   2656  CD  PRO   278      44.824  38.778  63.311  1.00 57.20      AAAA C
ATOM   2657  CA  PRO   278      42.946  38.185  61.899  1.00 55.82      AAAA C
ATOM   2658  CB  PRO   278      42.445  38.635  63.267  1.00 55.61      AAAA C
ATOM   2659  CG  PRO   278      43.605  38.670  64.153  1.00 55.58      AAAA C
ATOM   2660  C   PRO   278      42.487  39.116  60.781  1.00 52.55      AAAA C
ATOM   2661  O   PRO   278      43.083  40.195  60.631  1.00 48.76      AAAA O
ATOM   2662  N   SER   279      41.370  38.845  60.143  1.00 49.35      AAAA N
ATOM   2664  CA  SER   279      40.815  39.720  59.140  1.00 52.03      AAAA C
ATOM   2665  CB  SER   279      39.280  39.572  58.975  1.00 47.62      AAAA C
ATOM   2666  OG  SER   279      39.320  38.778  57.785  1.00 68.16      AAAA O
ATOM   2668  C   SER   279      41.003  41.209  59.173  1.00 55.40      AAAA C
ATOM   2669  O   SER   279      41.225  41.740  58.059  1.00 55.40      AAAA O
ATOM   2670  N   GLY   280      40.775  41.962  60.247  1.00 55.32      AAAA N
ATOM   2672  CA  GLY   280      40.968  43.406  59.868  1.00 48.58      AAAA C
ATOM   2673  C   GLY   280      42.248  43.890  60.479  1.00 55.98      AAAA C
ATOM   2674  O   GLY   280      42.249  45.097  60.772  1.00 56.00      AAAA O
ATOM   2675  N   PHE   281      43.213  42.983  60.742  1.00 55.42      AAAA N
ATOM   2677  CA  PHE   281      44.506  43.411  61.262  1.00 52.94      AAAA C
ATOM   2678  CB  PHE   281      44.938  42.644  62.523  1.00 61.20      AAAA C
ATOM   2679  CG  PHE   281      43.958  42.792  63.637  1.00 53.66      AAAA C
ATOM   2680  CD1 PHE   281      44.142  43.702  64.630  1.00 60.47      AAAA C
ATOM   2681  CD2 PHE   281      42.939  41.992  63.712  1.00 60.99      AAAA C
ATOM   2682  CE1 PHE   281      43.272  43.901  65.678  1.00 64.71      AAAA C
ATOM   2683  CE2 PHE   281      41.931  42.162  64.756  1.00 63.18      AAAA C
ATOM   2684  CZ  PHE   281      42.141  43.115  65.744  1.00 58.88      AAAA C
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ATOM   2685  C   PHE   281      45.630  43.217  60.240  1.00 48.00      AAAA C
ATOM   2686  O   PHE   281      45.738  42.395  59.327  1.00 38.84      AAAA O
ATOM   2687  N   ILE   282      46.670  43.990  60.557  1.00 49.55      AAAA N
ATOM   2689  CA  ILE   282      47.907  43.984  59.748  1.00 45.00      AAAA C
ATOM   2690  CB  ILE   282      47.945  45.188  58.799  1.00 30.25      AAAA C
ATOM   2691  CG2 ILE   282      48.041  46.494  59.507  1.00 24.60      AAAA C
ATOM   2692  CG1 ILE   282      49.092  45.022  57.795  1.00 38.71      AAAA C
ATOM   2693  CD1 ILE   282      49.194  46.043  56.669  1.00 33.38      AAAA C
ATOM   2694  C   ILE   282      49.081  43.889  60.673  1.00 44.30      AAAA C
ATOM   2695  O   ILE   282      49.078  44.447  61.759  1.00 48.49      AAAA O
ATOM   2696  N   ARG   283      50.126  43.153  60.298  1.00 48.68      AAAA N
ATOM   2698  CA  ARG   283      51.396  43.094  61.048  1.00 39.30      AAAA C
ATOM   2699  CB  ARG   283      52.300  42.200  60.286  1.00 41.10      AAAA C
ATOM   2700  CG  ARG   283      52.295  40.696  60.515  1.00 29.19      AAAA C
ATOM   2701  CD  ARG   283      53.078  39.986  59.451  1.00 29.85      AAAA C
ATOM   2702  NE  ARG   283      52.823  38.545  59.404  1.00 29.39      AAAA N
ATOM   2704  CZ  ARG   283      51.862  38.024  58.646  1.00 37.61      AAAA C
ATOM   2705  NH1 ARG   283      51.065  38.846  57.944  1.00 31.41      AAAA N
ATOM   2708  NH2 ARG   283      51.651  36.722  58.596  1.00 31.97      AAAA N
ATOM   2711  C   ARG   283      51.945  44.498  61.190  1.00 42.27      AAAA C
ATOM   2712  O   ARG   283      51.931  45.228  60.173  1.00 43.42      AAAA O
ATOM   2713  N   ASN   284      52.362  44.886  62.422  1.00 39.49      AAAA N
ATOM   2715  CA  ASN   284      52.733  46.311  62.574  1.00 42.07      AAAA C
ATOM   2721  C   ASN   284      54.078  46.656  61.929  1.00 41.64      AAAA C
ATOM   2722  O   ASN   284      54.431  47.798  61.742  1.00 39.01      AAAA O
ATOM   2716  CB  ASN   284      52.734  46.760  64.032  1.00 37.33      AAAA C
ATOM   2717  CG  ASN   284      53.917  46.028  64.611  1.00 50.21      AAAA C
ATOM   2718  OD1 ASN   284      54.609  45.104  64.192  1.00 44.30      AAAA O
ATOM   2719  ND2 ASN   284      54.323  46.432  65.842  1.00 42.46      AAAA N
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ATOM   2725  CA  GLY   285      55.971  45.815  60.593  1.00 26.91      AAAA C
ATOM   2726  C   GLY   285      56.091  44.468  59.848  1.00 33.12      AAAA C
ATOM   2727  O   GLY   285      55.584  43.331  60.187  1.00 29.51      AAAA O
ATOM   2728  N   SER   286      56.915  44.619  58.766  1.00 26.53      AAAA N
ATOM   2730  CA  SER   286      57.109  43.385  57.975  1.00 32.67      AAAA C
ATOM   2731  CB  SER   286      57.944  43.681  56.757  1.00 33.19      AAAA C
ATOM   2732  OG  SER   286      58.283  42.480  56.014  1.00 31.95      AAAA O
ATOM   2734  C   SER   286      57.750  42.310  58.836  1.00 34.57      AAAA C
ATOM   2735  O   SER   286      58.700  42.495  59.607  1.00 44.29      AAAA O
ATOM   2736  N   GLN   287      57.227  41.148  58.940  1.00 34.45      AAAA N
ATOM   2738  CA  GLN   287      57.738  40.005  59.634  1.00 35.25      AAAA C
ATOM   2739  CB  GLN   287      59.139  39.610  59.083  1.00 27.97      AAAA C
ATOM   2740  CG  GLN   287      59.037  39.234  57.664  1.00 26.61      AAAA C
ATOM   2741  CD  GLN   287      58.539  37.963  57.130  1.00 21.25      AAAA C
ATOM   2742  OE1 GLN   287      58.192  37.023  57.845  1.00 28.18      AAAA O
ATOM   2743  NE2 GLN   287      58.492  37.838  55.782  1.00 27.55      AAAA N
ATOM   2746  C   GLN   287      57.773  40.286  61.111  1.00 30.25      AAAA C
ATOM   2747  O   GLN   287      58.163  39.415  61.908  1.00 32.78      AAAA O
ATOM   2748  N   SER   288      57.021  41.217  61.624  1.00 32.49      AAAA N
ATOM   2750  CA  SER   288      56.696  41.322  63.043  1.00 28.98      AAAA C
ATOM   2751  CB  SER   288      56.024  42.675  63.313  1.00 35.79      AAAA C
ATOM   2752  OG  SER   288      55.639  42.612  64.701  1.00 36.61      AAAA O
ATOM   2754  C   SER   288      55.665  40.285  63.442  1.00 28.96      AAAA C
ATOM   2755  O   SER   288      54.993  39.776  62.553  1.00 31.16      AAAA O
ATOM   2756  N   MET   289      55.774  39.720  64.621  1.00 32.51      AAAA N
ATOM   2758  CA  MET   289      54.875  38.697  65.105  1.00 34.53      AAAA C
ATOM   2759  CB  MET   289      55.507  37.823  66.153  1.00 30.31      AAAA C
ATOM   2760  CG  MET   289      56.571  36.872  65.680  1.00 40.50      AAAA C
ATOM   2761  SD  MET   289      56.977  35.623  66.881  1.00 31.65      AAAA S
ATOM   2762  CE  MET   289      55.745  34.315  66.508  1.00 30.47      AAAA C
ATOM   2763  C   MET   289      53.557  39.286  65.703  1.00 35.55      AAAA C
ATOM   2764  O   MET   289      52.630  38.512  66.014  1.00 38.37      AAAA O
ATOM   2765  N   TYR   290      53.380  40.565  65.742  1.00 29.54      AAAA N
ATOM   2767  CA  TYR   290      52.363  41.358  66.297  1.00 38.81      AAAA C
ATOM   2768  CB  TYR   290      52.947  42.589  67.042  1.00 36.72      AAAA C
ATOM   2769  CG  TYR   290      53.570  42.184  68.351  1.00 41.94      AAAA C
ATOM   2770  CD1 TYR   290      54.932  41.780  68.350  1.00 37.79      AAAA C
ATOM   2771  CE1 TYR   290      55.548  41.368  69.503  1.00 32.60      AAAA C
ATOM   2772  CD2 TYR   290      52.887  42.157  69.570  1.00 39.93      AAAA C
ATOM   2773  CE2 TYR   290      53.501  41.750  70.748  1.00 36.16      AAAA C
ATOM   2774  CZ  TYR   290      54.822  41.355  70.693  1.00 38.85      AAAA C
ATOM   2775  OH  TYR   290      55.581  40.923  71.751  1.00 43.41      AAAA O
ATOM   2777  C   TYR   290      51.361  41.955  65.270  1.00 45.54      AAAA C
ATOM   2778  O   TYR   290      51.733  42.520  64.227  1.00 47.10      AAAA O
ATOM   2779  N   CYS   291      50.071  41.698  65.537  1.00 44.68      AAAA N
ATOM   2781  CA  CYS   291      49.017  42.205  64.685  1.00 47.20      AAAA C
ATOM   2782  C   CYS   291      48.295  43.434  65.194  1.00 46.06      AAAA C
ATOM   2783  O   CYS   291      47.892  43.550  66.343  1.00 49.45      AAAA O
ATOM   2784  CB  CYS   291      47.973  41.103  64.483  1.00 43.44      AAAA C
ATOM   2785  SG  CYS   291      48.766  39.715  63.683  1.00 45.49      AAAA S
ATOM   2786  N   ILE   292      48.136  44.453  64.365  1.00 46.82      AAAA N
ATOM   2788  CA  ILE   292      47.399  45.651  64.755  1.00 50.64      AAAA C
ATOM   2789  CB  ILE   292      48.267  46.932  64.779  1.00 39.19      AAAA C
ATOM   2790  CG2 ILE   292      49.291  46.885  65.861  1.00 44.39      AAAA C
ATOM   2791  CG1 ILE   292      48.920  47.095  63.402  1.00 44.25      AAAA C
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ATOM   2792  CD1 ILE   292      49.234  48.568  63.108  1.00 32.80      AAAA C
ATOM   2793  C   ILE   292      46.240  46.003  63.806  1.00 50.01      AAAA C
ATOM   2794  O   ILE   292      46.165  45.526  62.670  1.00 46.64      AAAA O
ATOM   2795  N   PRO   293      45.150  46.507  64.385  1.00 51.86      AAAA N
ATOM   2796  CD  PRO   293      45.009  46.804  65.839  1.00 51.05      AAAA C
ATOM   2797  CA  PRO   293      43.958  46.930  63.675  1.00 51.40      AAAA C
ATOM   2798  CB  PRO   293      43.170  47.784  64.681  1.00 49.00      AAAA C
ATOM   2799  CG  PRO   293      43.533  47.112  65.951  1.00 53.73      AAAA C
ATOM   2800  C   PRO   293      44.253  47.870  62.525  1.00 51.68      AAAA C
ATOM   2801  O   PRO   293      45.053  48.788  62.737  1.00 51.92      AAAA O
ATOM   2802  N   CYS   294      43.607  47.621  61.408  1.00 50.66      AAAA N
ATOM   2804  CA  CYS   294      43.811  48.464  60.254  1.00 57.90      AAAA C
ATOM   2805  C   CYS   294      43.219  49.848  60.345  1.00 59.59      AAAA C
ATOM   2806  O   CYS   294      43.744  50.814  59.785  1.00 60.87      AAAA O
ATOM   2807  CB  CYS   294      43.229  47.686  59.046  1.00 57.59      AAAA C
ATOM   2808  SG  CYS   294      44.408  46.460  58.563  1.00 51.12      AAAA S
ATOM   2809  N   ALA   295      42.009  50.031  60.854  1.00 65.87      AAAA N
ATOM   2811  CA  ALA   295      41.391  51.386  60.804  1.00 71.19      AAAA C
ATOM   2812  CB  ALA   295      42.311  52.459  61.393  1.00 63.82      AAAA C
ATOM   2813  C   ALA   295      40.971  51.770  59.370  1.00 69.17      AAAA C
ATOM   2814  O   ALA   295      41.421  52.717  58.762  1.00 64.70      AAAA O
ATOM   2815  N   GLY   296      40.153  50.920  58.775  1.00 71.30      AAAA N
ATOM   2817  CA  GLY   296      39.640  51.049  57.416  1.00 72.66      AAAA C
ATOM   2818  C   GLY   296      39.895  49.686  56.769  1.00 74.20      AAAA C
ATOM   2819  O   GLY   296      40.408  48.819  57.490  1.00 75.04      AAAA O
ATOM   2820  N   PRO   297      39.561  49.540  55.497  1.00 71.98      AAAA N
ATOM   2821  CD  PRO   297      38.928  50.561  54.637  1.00 72.15      AAAA C
ATOM   2822  CA  PRO   297      39.958  48.344  54.777  1.00 68.23      AAAA C
ATOM   2823  CB  PRO   297      39.488  48.603  53.369  1.00 72.57      AAAA C
ATOM   2824  CG  PRO   297      38.470  49.687  53.490  1.00 74.04      AAAA C
ATOM   2825  C   PRO   297      41.480  48.306  54.860  1.00 65.78      AAAA C
ATOM   2826  O   PRO   297      42.147  49.323  54.997  1.00 62.72      AAAA O
ATOM   2827  N   CYS   298      42.039  47.135  55.073  1.00 63.85      AAAA N
ATOM   2829  CA  CYS   298      43.464  46.953  55.248  1.00 54.47      AAAA C
ATOM   2830  C   CYS   298      44.109  47.303  53.908  1.00 54.56      AAAA C
ATOM   2831  O   CYS   298      43.621  47.030  52.820  1.00 54.83      AAAA O
ATOM   2832  CB  CYS   298      43.665  45.544  55.669  1.00 47.65      AAAA C
ATOM   2833  SG  CYS   298      43.501  45.115  57.371  1.00 46.12      AAAA S
ATOM   2834  N   PRO   299      45.310  47.876  53.967  1.00 49.83      AAAA N
ATOM   2835  CD  PRO   299      46.087  48.168  55.194  1.00 48.14      AAAA C
ATOM   2836  CA  PRO   299      46.055  48.212  52.787  1.00 43.67      AAAA C
ATOM   2837  CB  PRO   299      47.267  48.965  53.281  1.00 44.08      AAAA C
ATOM   2838  CG  PRO   299      47.454  48.361  54.628  1.00 51.38      AAAA C
ATOM   2839  C   PRO   299      46.341  46.969  52.010  1.00 38.86      AAAA C
ATOM   2840  O   PRO   299      46.372  45.874  52.546  1.00 42.85      AAAA O
ATOM   2841  N   LYS   300      46.310  47.073  50.712  1.00 38.30      AAAA N
ATOM   2843  CA  LYS   300      46.484  45.958  49.812  1.00 42.62      AAAA C
ATOM   2844  CB  LYS   300      45.176  45.226  49.595  1.00 34.28      AAAA C
ATOM   2845  CG  LYS   300      45.346  43.901  48.920  1.00 41.45      AAAA C
ATOM   2846  CD  LYS   300      44.013  43.413  48.378  1.00 48.31      AAAA C
ATOM   2847  CE  LYS   300      44.388  42.027  47.787  1.00 48.57      AAAA C
ATOM   2848  NZ  LYS   300      43.662  42.031  46.478  1.00 63.70      AAAA N
ATOM   2852  C   LYS   300      46.964  46.479  48.432  1.00 48.72      AAAA C
ATOM   2853  O   LYS   300      46.413  47.383  47.776  1.00 46.09      AAAA O
ATOM   2854  N   VAL   301      48.150  45.984  48.054  1.00 48.15      AAAA N
ATOM   2856  CA  VAL   301      48.802  46.462  46.871  1.00 44.52      AAAA C
ATOM   2857  CB  VAL   301      50.292  46.729  47.074  1.00 51.52      AAAA C
ATOM   2858  CG1 VAL   301      51.008  47.200  45.796  1.00 43.07      AAAA C
ATOM   2859  CG2 VAL   301      50.495  47.794  48.141  1.00 49.50      AAAA C
ATOM   2860  C   VAL   301      48.526  45.410  45.837  1.00 44.59      AAAA C
ATOM   2861  O   VAL   301      48.913  44.291  46.060  1.00 43.70      AAAA O
ATOM   2862  N   CYS   302      47.910  45.816  44.718  1.00 47.98      AAAA N
ATOM   2864  CA  CYS   302      47.645  44.735  43.739  1.00 55.19      AAAA C
ATOM   2865  C   CYS   302      48.594  44.968  42.583  1.00 57.64      AAAA C
ATOM   2866  O   CYS   302      48.852  46.152  42.343  1.00 60.23      AAAA O
ATOM   2867  CB  CYS   302      46.186  44.630  43.330  1.00 68.30      AAAA C
ATOM   2868  SG  CYS   302      45.070  44.360  44.751  1.00 70.31      AAAA S
ATOM   2869  N   GLU   303      49.183  43.921  42.075  1.00 58.15      AAAA N
ATOM   2871  CA  GLU   303      50.174  43.932  41.034  1.00 62.85      AAAA C
ATOM   2872  CB  GLU   303      51.603  44.006  41.595  1.00 67.85      AAAA C
ATOM   2873  CG  GLU   303      51.760  43.487  43.014  0.01 67.46      AAAA C
ATOM   2874  CD  GLU   303      51.989  41.992  43.097  0.01 67.94      AAAA C
ATOM   2875  OE1 GLU   303      53.011  41.514  42.561  0.01 67.67      AAAA O
ATOM   2876  OE2 GLU   303      51.147  41.290  43.697  0.01 67.65      AAAA O
ATOM   2877  C   GLU   303      50.096  42.662  40.194  1.00 64.12      AAAA C
ATOM   2878  O   GLU   303      50.162  41.562  40.708  1.00 65.08      AAAA O
ATOM   2879  N   GLU   304      49.867  42.794  38.904  1.00 67.37      AAAA N
ATOM   2881  CA  GLU   304      49.672  41.583  38.094  1.00 74.63      AAAA C
ATOM   2882  CB  GLU   304      48.285  41.596  37.458  1.00 71.71      AAAA C
ATOM   2983  CG  GLU   304      47.339  42.663  38.031  1.00 84.54      AAAA C
ATOM   2884  CD  GLU   304      45.930  42.152  38.135  1.00 87.56      AAAA C
ATOM   2885  OE1 GLU   304      45.438  41.571  37.179  1.00 89.13      AAAA O
ATOM   2886  OE2 GLU   304      45.249  42.269  39.233  1.00 93.19      AAAA O
ATOM   2887  C   GLU   304      50.866  41.307  37.190  1.00 76.10      AAAA C
ATOM   2888  O   GLU   304      51.911  41.962  37.217  1.00 74.78      AAAA O
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ATOM   2889  N   GLU   305      50.899  40.126  36.568  1.00 77.31      AAAA N
ATOM   2991  CA  GLU   305      51.932  39.656  35.674  1.00 75.90      AAAA C
ATOM   2892  CB  GLU   305      51.467  38.380  34.970  1.00 79.95      AAAA C
ATOM   2993  CG  GLU   305      52.307  37.937  33.807  1.00 87.28      AAAA C
ATOM   2894  CD  GLU   305      51.758  36.891  32.886  0.01 83.39      AAAA C
ATOM   2895  OE1 GLU   305      50.762  36.234  33.252  0.01 83.66      AAAA O
ATOM   2896  OE2 GLU   305      52.310  36.700  31.780  0.01 83.73      AAAA O
ATOM   2897  C   GLU   305      52.276  40.737  34.666  1.00 75.97      AAAA C
ATOM   2898  O   GLU   305      53.381  41.268  34.613  1.00 76.54      AAAA O
ATOM   2899  N   LYS   306      51.291  41.181  33.888  1.00 78.22      AAAA N
ATOM   2901  CA  LYS   306      51.479  42.328  33.004  1.00 75.99      AAAA C
ATOM   2902  CB  LYS   306      50.467  42.253  31.855  1.00 79.78      AAAA C
ATOM   2903  CG  LYS   306      51.208  42.227  30.527  1.00 94.52      AAAA C
ATOM   2904  CD  LYS   306      50.313  42.191  29.314  1.00 92.78      AAAA C
ATOM   2905  CE  LYS   306      50.740  43.227  28.261  1.00 97.10      AAAA C
ATOM   2906  NZ  LYS   306      50.938  44.554  28.929  1.00 84.87      AAAA N
ATOM   2910  C   LYS   306      51.381  43.669  33.703  1.00 73.85      AAAA C
ATOM   2911  O   LYS   306      50.703  43.862  34.718  1.00 76.08      AAAA O
ATOM   2912  N   LYS   307      52.000  44.700  33.180  1.00 71.15      AAAA N
ATOM   2914  CA  LYS   307      51.934  46.053  33.692  1.00 69.45      AAAA C
ATOM   2915  CB  LYS   307      53.022  46.903  33.008  1.00 79.64      AAAA C
ATOM   2916  CG  LYS   307      54.419  46.837  33.564  1.00 78.88      AAAA C
ATOM   2917  CD  LYS   307      55.257  48.084  33.374  1.00 85.84      AAAA C
ATOM   2918  CE  LYS   307      55.708  48.215  31.924  1.00 97.07      AAAA C
ATOM   2919  NZ  LYS   307      54.649  48.840  31.067  1.00 97.80      AAAA N
ATOM   2923  C   LYS   307      50.562  46.716  33.525  1.00 67.97      AAAA C
ATOM   2924  O   LYS   307      50.010  47.369  34.431  1.00 64.46      AAAA O
ATOM   2925  N   THR   308      49.979  46.661  32.323  1.00 65.84      AAAA N
ATOM   2927  CA  THR   308      48.709  47.319  32.091  1.00 64.56      AAAA C
ATOM   2928  CB  THR   308      48.714  47.977  30.711  1.00 59.91      AAAA C
ATOM   2929  OG1 THR   308      49.834  48.843  30.577  1.00 61.97      AAAA O
ATOM   2931  CG2 THR   308      47.392  48.742  30.561  1.00 63.64      AAAA C
ATOM   2932  C   THR   308      47.514  46.379  32.234  1.00 61.82      AAAA C
ATOM   2933  O   THR   308      47.412  45.415  31.477  1.00 62.05      AAAA O
ATOM   2934  N   LYS   309      46.675  46.719  33.211  1.00 55.66      AAAA N
ATOM   2936  CA  LYS   309      45.456  45.926  33.445  1.00 54.67      AAAA C
ATOM   2937  CB  LYS   309      45.043  45.880  34.904  1.00 56.82      AAAA C
ATOM   2938  CG  LYS   309      43.601  45.541  35.223  1.00 57.50      AAAA C
ATOM   2939  CD  LYS   309      43.390  44.039  35.086  1.00 59.50      AAAA C
ATOM   2940  CE  LYS   309      42.703  43.448  36.324  1.00 57.31      AAAA C
ATOM   2941  NZ  LYS   309      42.758  41.954  36.236  1.00 57.22      AAAA N
ATOM   2945  C   LYS   309      44.391  46.570  32.548  1.00 51.21      AAAA C
ATOM   2946  O   LYS   309      44.074  47.763  32.680  1.00 47.23      AAAA O
ATOM   2947  N   THR   310      43.895  45.772  31.610  1.00 47.67      AAAA N
ATOM   2949  CA  THR   310      42.862  46.328  30.733  1.00 51.89      AAAA C
ATOM   2950  CB  THR   310      43.161  46.015  29.266  1.00 54.81      AAAA C
ATOM   2951  OG1 THR   310      41.909  45.710  28.635  1.00 66.29      AAAA O
ATOM   2953  CG2 THR   310      44.032  44.791  29.139  1.00 55.18      AAAA C
ATOM   2954  C   THR   310      41.468  45.841  31.117  1.00 51.15      AAAA C
ATOM   2955  O   THR   310      41.162  44.680  30.991  1.00 49.27      AAAA O
ATOM   2956  N   ILE   311      40.684  46.706  31.732  1.00 50.18      AAAA N
ATOM   2958  CA  ILE   311      39.363  46.453  32.276  1.00 48.67      AAAA C
ATOM   2959  CB  ILE   311      39.120  47.396  33.462  1.00 49.27      AAAA C
ATOM   2960  CG2 ILE   311      37.655  47.596  33.799  1.00 50.72      AAAA C
ATOM   2961  CG1 ILE   311      39.896  46.930  34.699  1.00 41.34      AAAA C
ATOM   2962  CD1 ILE   311      39.847  48.073  35.739  1.00 52.22      AAAA C
ATOM   2963  C   ILE   311      38.334  46.729  31.186  1.00 45.37      AAAA C
ATOM   2964  O   ILE   311      38.132  47.875  30.758  1.00 37.14      AAAA O
ATOM   2965  N   ASP   312      37.871  45.678  30.524  1.00 50.10      AAAA N
ATOM   2967  CA  ASP   312      36.991  45.842  29.377  1.00 56.35      AAAA C
ATOM   2968  CB  ASP   312      37.546  45.152  28.128  1.00 59.45      AAAA C
ATOM   2969  CG  ASP   312      37.761  43.671  28.382  1.00 65.64      AAAA C
ATOM   2970  OD1 ASP   312      38.525  43.034  27.636  1.00 72.60      AAAA O
ATOM   2971  OD2 ASP   312      37.154  43.176  29.348  1.00 66.86      AAAA O
ATOM   2972  C   ASP   312      35.589  45.337  29.693  1.00 59.39      AAAA C
ATOM   2973  O   ASP   312      34.729  45.007  28.867  1.00 61.00      AAAA O
ATOM   2974  N   SER   313      35.278  45.290  30.976  1.00 61.17      AAAA N
ATOM   2976  CA  SER   313      34.053  44.683  31.459  1.00 55.73      AAAA C
ATOM   2977  CB  SER   313      34.121  43.201  31.093  1.00 48.22      AAAA C
ATOM   2978  OG  SER   313      34.373  42.514  32.282  1.00 57.89      AAAA O
ATOM   2980  C   SER   313      33.998  44.818  32.941  1.00 57.87      AAAA C
ATOM   2981  O   SER   313      34.802  45.506  33.537  1.00 66.47      AAAA O
ATOM   2982  N   VAL   314      33.001  44.205  33.545  1.00 64.35      AAAA N
ATOM   2984  CA  VAL   314      32.849  44.305  35.016  1.00 64.39      AAAA C
ATOM   2985  CB  VAL   314      31.360  44.340  35.343  1.00 69.57      AAAA C
ATOM   2986  CG1 VAL   314      31.024  43.693  36.681  1.00 65.60      AAAA C
ATOM   2987  CG2 VAL   314      30.927  45.823  35.319  1.00 65.27      AAAA C
ATOM   2988  C   VAL   314      33.492  43.088  35.638  1.00 62.65      AAAA C
ATOM   2989  O   VAL   314      34.029  43.141  36.704  1.00 63.92      AAAA O
ATOM   2990  N   THR   315      33.468  42.011  34.878  1.00 61.82      AAAA N
ATOM   2992  CA  THR   315      34.029  40.752  35.284  1.00 63.44      AAAA C
ATOM   2993  CB  THR   315      33.618  39.628  34.314  1.00 65.54      AAAA C
ATOM   2994  OG1 THR   315      32.403  40.004  33.634  1.00 74.05      AAAA O
ATOM   2996  CG2 THR   315      33.339  38.366  35.104  1.00 64.86      AAAA C
ATOM   2997  C   THR   315      35.541  40.871  35.323  1.00 65.62      AAAA C
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ATOM   2998  O   THR   315      36.217  40.339  36.206  1.00 66.41      AAAA O
ATOM   2999  N   SER   316      36.071  41.593  34.332  1.00 63.28      AAAA N
ATOM   3001  CA  SER   316      37.500  41.793  34.215  1.00 58.72      AAAA C
ATOM   3002  CB  SER   316      37.785  42.537  32.900  1.00 52.20      AAAA C
ATOM   3003  OG  SER   316      37.298  43.859  32.933  1.00 48.04      AAAA O
ATOM   3005  C   SER   316      38.077  42.573  35.387  1.00 58.91      AAAA C
ATOM   3006  O   SER   316      39.293  42.522  35.520  1.00 59.86      AAAA O
ATOM   3007  N   ALA   317      37.310  43.362  36.111  1.00 55.86      AAAA N
ATOM   3009  CA  ALA   317      37.750  44.184  37.191  1.00 57.17      AAAA C
ATOM   3010  CB  ALA   317      36.833  45.409  37.269  1.00 54.23      AAAA C
ATOM   3011  C   ALA   317      37.689  43.487  38.538  1.00 62.05      AAAA C
ATOM   3012  O   ALA   317      37.702  44.128  39.599  1.00 60.30      AAAA O
ATOM   3013  N   GLN   318      37.361  42.205  38.523  1.00 67.91      AAAA N
ATOM   3015  CA  GLN   318      37.185  41.380  39.713  1.00 70.72      AAAA C
ATOM   3016  CB  GLN   318      36.857  39.956  39.293  1.00 74.48      AAAA C
ATOM   3017  CG  GLN   318      36.624  38.947  40.383  1.00 89.82      AAAA C
ATOM   3018  CD  GLN   318      35.265  39.080  41.048  1.00 92.69      AAAA C
ATOM   3019  OE1 GLN   318      34.256  38.807  40.391  1.00 98.57      AAAA O
ATOM   3020  NE2 GLN   318      35.356  39.509  42.308  1.00 92.51      AAAA N
ATOM   3023  C   GLN   318      38.380  41.413  40.653  1.00 72.63      AAAA C
ATOM   3024  O   GLN   318      38.294  41.855  41.804  1.00 68.92      AAAA O
ATOM   3025  N   MET   319      39.562  41.062  40.153  1.00 75.18      AAAA N
ATOM   3027  CA  MET   319      40.846  41.175  40.826  1.00 71.85      AAAA C
ATOM   3028  CB  MET   319      41.950  40.960  39.772  1.00 82.00      AAAA C
ATOM   3029  CG  MET   319      41.740  39.644  39.050  1.00 91.16      AAAA C
ATOM   3030  SD  MET   319      43.123  38.482  39.185  1.00106.72      AAAA S
ATOM   3031  CE  MET   319      42.486  37.105  38.231  1.00 97.56      AAAA C
ATOM   3032  C   MET   319      41.118  42.509  41.471  1.00 67.68      AAAA C
ATOM   3033  O   MET   319      41.507  42.541  42.612  1.00 69.73      AAAA O
ATOM   3034  N   LEU   320      40.740  43.639  40.887  1.00 62.95      AAAA N
ATOM   3036  CA  LEU   320      40.907  44.938  41.531  1.00 62.31      AAAA C
ATOM   3037  CB  LEU   320      40.440  46.085  40.623  1.00 54.93      AAAA C
ATOM   3038  CG  LEU   320      41.091  46.163  39.238  1.00 53.48      AAAA C
ATOM   3039  CD1 LEU   320      41.005  47.552  38.692  1.00 51.31      AAAA C
ATOM   3040  CD2 LEU   320      42.557  45.709  39.403  1.00 58.43      AAAA C
ATOM   3041  C   LEU   320      40.209  45.008  42.881  1.00 60.30      AAAA C
ATOM   3042  O   LEU   320      40.344  45.969  43.661  1.00 58.72      AAAA O
ATOM   3043  N   GLN   321      39.267  44.106  43.112  1.00 59.62      AAAA N
ATOM   3045  CA  GLN   321      38.482  44.128  44.343  1.00 63.50      AAAA C
ATOM   3046  CB  GLN   321      37.373  43.089  44.250  1.00 62.52      AAAA C
ATOM   3047  CG  GLN   321      36.611  42.854  45.522  1.00 56.83      AAAA C
ATOM   3048  CD  GLN   321      35.337  42.064  45.291  1.00 68.77      AAAA C
ATOM   3049  OE1 GLN   321      35.362  40.969  44.718  1.00 70.37      AAAA O
ATOM   3050  NE2 GLN   321      34.218  42.632  45.764  1.00 63.77      AAAA N
ATOM   3053  C   GLN   321      39.367  44.030  45.594  1.00 60.97      AAAA C
ATOM   3054  O   GLN   321      40.262  43.196  45.782  1.00 57.29      AAAA O
ATOM   3055  N   GLY   322      39.092  44.928  46.546  1.00 57.62      AAAA N
ATOM   3057  CA  GLY   322      39.855  44.928  47.790  1.00 60.63      AAAA C
ATOM   3058  C   GLY   322      41.126  45.773  47.812  1.00 61.78      AAAA C
ATOM   3059  O   GLY   322      41.584  46.198  48.889  1.00 60.16      AAAA O
ATOM   3060  N   CYS   323      41.719  46.124  46.676  1.00 60.03      AAAA N
ATOM   3062  CA  CYS   323      42.938  46.845  46.528  1.00 54.20      AAAA C
ATOM   3063  C   CYS   323      42.924  48.307  46.910  1.00 53.48      AAAA C
ATOM   3064  O   CYS   323      42.105  49.148  46.503  1.00 56.43      AAAA O
ATOM   3065  CB  CYS   323      43.458  46.822  45.086  1.00 53.33      AAAA C
ATOM   3066  SG  CYS   323      43.325  45.222  44.248  1.00 66.22      AAAA S
ATOM   3067  N   THR   324      43.994  48.718  47.580  1.00 49.83      AAAA N
ATOM   3069  CA  THR   324      44.164  50.161  47.811  1.00 52.29      AAAA C
ATOM   3070  CB  THR   324      44.623  50.324  49.264  1.00 52.84      AAAA C
ATOM   3071  OG1 THR   324      45.245  49.087  49.634  1.00 59.82      AAAA O
ATOM   3073  CG2 THR   324      43.432  50.517  50.193  1.00 60.00      AAAA C
ATOM   3074  C   THR   324      45.154  50.802  46.844  1.00 48.91      AAAA C
ATOM   3075  O   THR   324      45.277  52.016  46.710  1.00 46.90      AAAA O
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ATOM   3078  CA  ILE   325      47.114  50.511  45.445  1.00 45.10      AAAA C
ATOM   3079  CB  ILE   325      48.473  50.577  46.183  1.00 43.60      AAAA C
ATOM   3080  CG2 ILE   325      49.586  50.905  45.163  1.00 47.47      AAAA C
ATOM   3081  CG1 ILE   325      48.394  51.623  47.294  1.00 34.03      AAAA C
ATOM   3082  CD1 ILE   325      49.595  52.010  48.028  1.00 41.94      AAAA C
ATOM   3083  C   ILE   325      47.265  49.642  44.229  1.00 42.88      AAAA C
ATOM   3084  O   ILE   325      47.406  48.429  44.469  1.00 42.99      AAAA O
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ATOM   3088  CB  PHE   326      46.166  49.437  40.877  1.00 39.15      AAAA C
ATOM   3089  CG  PHE   326      46.403  48.474  39.738  1.00 38.03      AAAA C
ATOM   3090  CD1 PHE   326      46.186  47.125  39.951  1.00 39.68      AAAA C
ATOM   3091  CD2 PHE   326      46.917  48.892  38.525  1.00 37.31      AAAA C
ATOM   3092  CE1 PHE   326      46.447  46.139  39.023  1.00 36.52      AAAA C
ATOM   3093  CE2 PHE   326      47.136  47.919  37.551  1.00 45.74      AAAA C
ATOM   3094  CZ  PHE   326      46.924  46.570  37.787  1.00 39.92      AAAA C
ATOM   3095  C   PHE   326      48.682  49.673  41.280  1.00 48.78      AAAA C
ATOM   3096  O   PHE   326      49.024  50.826  40.966  1.00 51.39      AAAA O
ATOM   3097  N   LYS   327      49.623  48.751  41.379  1.00 50.22      AAAA N
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ATOM   3100  CB  LYS   327      52.050  48.091  41.519  1.00 58.64      AAAA C
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ATOM   3103  CE  LYS   327      55.400  48.951  40.592  1.00 68.12      AAAA C
ATOM   3104  NZ  LYS   327      56.260  47.889  39.938  1.00 71.97      AAAA N
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ATOM   3109  O   LYS   327      50.901  47.245  39.127  1.00 49.55      AAAA O
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ATOM   3114  O   GLY   328      49.858  51.307  36.881  1.00 31.92      AAAA O
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ATOM   3124  C   ASN   329      47.038  50.207  34.357  1.00 50.37      AAAA C
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ATOM   3131  CD1 LEU   330      42.864  51.924  37.417  1.00 38.12      AAAA C
ATOM   3132  CD2 LEU   330      43.283  49.565  36.669  1.00 38.74      AAAA C
ATOM   3133  C   LEU   330      44.352  51.377  32.758  1.00 39.10      AAAA C
ATOM   3134  O   LEU   330      44.509  52.545  32.460  1.00 40.71      AAAA O
ATOM   3135  N   LEU   331      43.933  50.516  31.904  1.00 36.10      AAAA N
ATOM   3137  CA  LEU   331      43.367  50.869  30.625  1.00 43.10      AAAA C
ATOM   3138  CB  LEU   331      43.958  49.894  29.585  1.00 42.29      AAAA C
ATOM   3139  CG  LEU   331      43.301  49.960  28.221  1.00 40.89      AAAA C
ATOM   3140  CD1 LEU   331      43.501  51.319  27.627  1.00 46.64      AAAA C
ATOM   3141  CD2 LEU   331      43.844  48.834  27.367  1.00 48.76      AAAA C
ATOM   3142  C   LEU   331      41.872  50.568  30.705  1.00 41.12      AAAA C
ATOM   3143  O   LEU   331      41.562  49.365  30.779  1.00 40.08      AAAA O
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ATOM   3148  CG2 ILE   332      37.413  51.612  32.195  1.00 34.66      AAAA C
ATOM   3149  CG1 ILE   332      39.550  51.895  33.452  1.00 33.64      AAAA C
ATOM   3150  CD1 ILE   332      39.479  53.152  34.337  1.00 48.21      AAAA C
ATOM   3151  C   ILE   332      38.959  51.367  29.688  1.00 34.03      AAAA C
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ATOM   3159  ND2 ASN   333      39.290  50.350  24.467  1.00 45.83      AAAA N
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ATOM   3163  O   ASN   333      36.462  48.409  27.398  1.00 44.40      AAAA O
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ATOM   3168  CG2 ILE   334      32.362  49.355  30.047  1.00 54.04      AAAA C
ATOM   3169  CG1 ILE   334      34.737  49.224  30.915  1.00 60.43      AAAA C
ATOM   3170  CD1 ILE   334      34.346  49.687  32.317  1.00 68.57      AAAA C
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ATOM   3175  CA  ARG   335      31.910  49.567  25.573  1.00 73.93      AAAA C
ATOM   3176  CB  ARG   335      32.262  48.903  24.240  1.00 74.44      AAAA C
ATOM   3177  CG  ARG   335      33.729  48.932  23.918  1.00 82.97      AAAA C
ATOM   3178  CD  ARG   335      34.102  49.289  22.500  1.00 86.49      AAAA C
ATOM   3179  NE  ARG   335      34.361  48.040  21.777  1.00 89.83      AAAA N
ATOM   3181  CZ  ARG   335      34.011  47.838  20.496  1.00 93.67      AAAA C
ATOM   3182  NH1 ARG   335      33.409  48.852  19.843  1.00 87.24      AAAA N
ATOM   3185  NH2 ARG   335      34.256  46.674  19.877  1.00 75.31      AAAA N
ATOM   3188  C   ARG   335      30.492  49.233  26.021  1.00 81.52      AAAA C
ATOM   3189  O   ARG   335      29.664  50.115  26.239  1.00 84.11      AAAA O
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ATOM   3193  CB  ALA   336      28.835  45.980  26.633  1.00 94.03      AAAA C
ATOM   3194  C   ALA   336      28.479  48.058  27.953  1.00 96.61      AAAA C
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ATOM   3198  CA  GLY   337      26.986  49.385  29.272  1.00103.11      AAAA C
ATOM   3199  C   GLY   337      25.568  49.303  29.763  1.00105.51      AAAA C
ATOM   3200  O   GLY   337      24.801  50.267  29.596  1.00106.64      AAAA O
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ATOM   3204  CB  ASN   338      23.714  46.689  31.624  1.00109.14      AAAA C
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ATOM   3206  OD1 ASN   338      25.598  45.595  30.625  1.00117.94      AAAA O
ATOM   3207  ND2 ASN   338      23.604  44.508  30.683  1.00113.72      AAAA N
ATOM   3210  C   ASN   338      23.790  49.160  31.931  1.00105.84      AAAA C
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ATOM   3215  CB  ASN   339      23.252  49.915  34.945  1.00109.15      AAAA C
ATOM   3216  CG  ASN   339      22.777  51.351  35.003  0.01107.52      AAAA C
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ATOM   3218  ND2 ASN   339      22.441  51.932  33.859  0.01107.46      AAAA N
ATOM   3221  C   ASN   339      25.697  49.237  35.007  1.00106.33      AAAA C
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ATOM   3228  CG1 ILE   340      29.726  49.158  33.070  1.00 85.50      AAAA C
ATOM   3229  CD1 ILE   340      28.897  49.634  31.915  1.00 92.53      AAAA C
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ATOM   3240  CA  SER   342      27.910  50.601  40.780  1.00 82.05      AAAA C
ATOM   3241  CB  SER   342      26.426  50.667  41.112  1.00 85.51      AAAA C
ATOM   3242  OG  SER   342      26.145  51.271  42.361  1.00 86.02      AAAA O
ATOM   3244  C   SER   342      28.487  49.196  40.965  1.00 76.62      AAAA C
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ATOM   3250  CG  GLU   343      27.118  46.105  38.316  1.00 85.33      AAAA C
ATOM   3251  CD  GLU   343      26.898  45.121  37.169  1.00 92.76      AAAA C
ATOM   3252  OE1 GLU   343      27.209  43.911  37.310  1.00 96.41      AAAA O
ATOM   3253  OE2 GLU   343      26.423  45.517  36.082  1.00 98.55      AAAA O
ATOM   3254  C   GLU   343      30.525  47.319  39.804  1.00 77.75      AAAA C
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ATOM   3259  CB  LEU   344      32.760  49.697  37.808  1.00 64.33      AAAA C
ATOM   3260  CG  LEU   344      32.687  49.397  36.311  1.00 50.12      AAAA C
ATOM   3261  CD1 LEU   344      33.224  50.577  35.519  1.00 57.00      AAAA C
ATOM   3262  CD2 LEU   344      33.401  48.127  35.905  1.00 51.62      AAAA C
ATOM   3263  C   LEU   344      32.963  49.130  40.174  1.00 69.74      AAAA C
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ATOM   3268  CB  GLU   345      31.592  51.714  42.478  1.00 55.59      AAAA C
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ATOM   3270  CD  GLU   345      31.324  53.374  44.376  1.00 81.31      AAAA C
ATOM   3271  OE1 GLU   345      30.614  54.320  43.976  1.00 85.60      AAAA O
ATOM   3272  OE2 GLU   345      31.237  53.078  45.595  1.00 88.79      AAAA O
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ATOM   3278  CB  ASN   346      31.024  46.498  44.095  1.00 61.66      AAAA C
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ATOM   3280  OD1 ASN   346      31.188  45.352  46.224  1.00 69.11      AAAA O
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ATOM   3301  CB  MET   348      37.402  50.096  40.493  1.00 31.72      AAAA C
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ATOM   3303  SD  MET   348      37.566  49.448  37.732  1.00 44.79      AAAA S
ATOM   3304  CE  MET   348      38.408  50.999  37.791  1.00 59.57      AAAA C
ATOM   3305  C   MET   348      37.368  50.831  42.867  1.00 45.88      AAAA C
ATOM   3306  O   MET   348      38.210  51.772  42.901  1.00 43.33      AAAA O
ATOM   3307  N   GLY   349      36.296  50.783  43.683  1.00 45.30      AAAA N
ATOM   3309  CA  GLY   349      35.998  51.965  44.504  1.00 49.19      AAAA C
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ATOM   3315  CB  LEU   350      38.873  49.949  47.834  1.00 49.00      AAAA C
ATOM   3316  CG  LEU   350      37.871  50.020  49.031  1.00 50.79      AAAA C
ATOM   3317  CD1 LEU   350      37.705  48.680  49.700  1.00 52.92      AAAA C
ATOM   3318  CD2 LEU   350      38.247  51.106  50.038  1.00 56.11      AAAA C
ATOM   3319  C   LEU   350      40.144  51.727  46.685  1.00 61.34      AAAA C
ATOM   3320  O   LEU   350      40.931  51.962  47.618  1.00 63.52      AAAA O
ATOM   3321  N   ILE   351      40.446  51.677  45.372  1.00 57.89      AAAA N
ATOM   3323  CA  ILE   351      41.729  52.088  44.873  1.00 48.69      AAAA C
ATOM   3324  CB  ILE   351      41.814  51.912  43.352  1.00 48.19      AAAA C
ATOM   3325  CG2 ILE   351      43.121  52.416  42.757  1.00 40.01      AAAA C
ATOM   3326  CG1 ILE   351      41.535  50.418  43.058  1.00 36.87      AAAA C
ATOM   3327  CD1 ILE   351      41.172  50.351  41.581  1.00 36.46      AAAA C
ATOM   3328  C   ILE   351      42.031  53.533  45.178  1.00 46.80      AAAA C
ATOM   3329  O   ILE   351      41.367  54.358  44.626  1.00 42.87      AAAA O
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ATOM   3332  CA  GLU   352      43.381  55.241  46.248  1.00 51.20      AAAA C
ATOM   3333  CB  GLU   352      43.907  55.353  47.678  1.00 52.12      AAAA C
ATOM   3334  CG  GLU   352      42.912  55.769  48.735  1.00 65.55      AAAA C
ATOM   3335  CD  GLU   352      43.034  54.834  49.947  1.00 71.49      AAAA C
ATOM   3336  OE1 GLU   352      43.881  55.244  50.765  1.00 66.09      AAAA O
ATOM   3337  OE2 GLU   352      42.330  53.799  50.009  1.00 76.07      AAAA O
ATOM   3338  C   GLU   352      44.502  55.751  45.314  1.00 47.43      AAAA C
ATOM   3339  O   GLU   352      44.798  56.951  45.182  1.00 40.38      AAAA O
ATOM   3340  N   VAL   353      45.342  54.838  44.852  1.00 43.54      AAAA N
ATOM   3342  CA  VAL   353      46.512  55.236  44.078  1.00 43.71      AAAA C
ATOM   3343  CB  VAL   353      47.759  55.540  44.911  1.00 45.01      AAAA C
ATOM   3344  CG1 VAL   353      47.766  55.261  46.387  1.00 30.84      AAAA C
ATOM   3345  CG2 VAL   353      48.988  54.844  44.310  1.00 42.55      AAAA C
ATOM   3346  C   VAL   353      46.828  54.233  42.957  1.00 41.41      AAAA C
ATOM   3347  O   VAL   353      46.843  53.003  43.172  1.00 39.19      AAAA O
ATOM   3348  N   VAL   354      47.074  54.855  41.816  1.00 36.31      AAAA N
ATOM   3350  CA  VAL   354      47.586  54.092  40.651  1.00 43.97      AAAA C
ATOM   3351  CB  VAL   354      46.725  54.390  39.407  1.00 40.86      AAAA C
ATOM   3352  CG1 VAL   354      47.347  53.896  38.123  1.00 36.72      AAAA C
ATOM   3353  CG2 VAL   354      45.293  53.849  39.678  1.00 35.35      AAAA C
ATOM   3354  C   VAL   354      49.043  54.510  40.388  1.00 44.56      AAAA C
ATOM   3355  O   VAL   354      49.366  55.718  40.288  1.00 43.32      AAAA O
ATOM   3356  N   THR   355      49.972  53.561  40.431  1.00 43.83      AAAA N
ATOM   3358  CA  THR   355      51.392  53.914  40.284  1.00 44.85      AAAA C
ATOM   3359  CB  THR   355      52.374  52.799  40.653  1.00 42.40      AAAA C
ATOM   3360  OG1 THR   355      52.273  51.744  39.695  1.00 45.30      AAAA O
ATOM   3362  CG2 THR   355      52.210  52.194  42.039  1.00 38.13      AAAA C
ATOM   3363  C   THR   355      51.746  54.339  38.851  1.00 43.84      AAAA C
ATOM   3364  O   THR   355      52.463  55.334  38.697  1.00 44.26      AAAA O
ATOM   3365  N   GLY   356      51.127  53.704  37.870  1.00 41.16      AAAA N
ATOM   3367  CA  GLY   356      51.358  54.073  36.470  1.00 37.81      AAAA C
ATOM   3368  C   GLY   356      50.505  55.204  35.955  1.00 38.07      AAAA C
ATOM   3369  O   GLY   356      50.364  56.261  36.615  1.00 34.65      AAAA O
ATOM   3370  N   TYR   357      49.910  55.004  34.800  1.00 38.47      AAAA N
ATOM   3372  CA  TYR   357      48.982  55.973  34.205  1.00 38.03      AAAA C
ATOM   3373  CB  TYR   357      49.557  56.343  32.805  1.00 31.44      AAAA C
ATOM   3374  CG  TYR   357      49.473  55.219  31.812  1.00 33.04      AAAA C
ATOM   3375  CD1 TYR   357      48.333  54.842  31.077  1.00 32.86      AAAA C
ATOM   3376  CE1 TYR   357      48.352  53.779  30.175  1.00 32.83      AAAA C
ATOM   3377  CD2 TYR   357      50.639  54.465  31.606  1.00 34.28      AAAA C
ATOM   3378  CE2 TYR   357      50.706  53.402  30.720  1.00 32.51      AAAA C
ATOM   3379  CZ  TYR   357      49.552  53.068  30.007  1.00 37.26      AAAA C
ATOM   3380  OH  TYR   357      49.726  51.997  29.166  1.00 35.85      AAAA O
ATOM   3382  C   TYR   357      47.582  55.368  34.150  1.00 38.55      AAAA C
ATOM   3383  O   TYR   357      47.458  54.127  34.088  1.00 36.11      AAAA O
ATOM   3384  N   VAL   358      46.593  56.216  33.814  1.00 40.98      AAAA N
ATOM   3386  CA  VAL   358      45.197  55.798  33.639  1.00 38.90      AAAA C
ATOM   3387  CB  VAL   358      44.211  56.502  34.610  1.00 49.15      AAAA C
ATOM   3388  CG1 VAL   358      42.815  55.883  34.484  1.00 33.12      AAAA C
ATOM   3389  CG2 VAL   358      44.748  56.437  36.043  1.00 29.20      AAAA C
ATOM   3390  C   VAL   358      44.760  56.194  32.234  1.00 35.64      AAAA C
ATOM   3391  O   VAL   358      44.792  57.358  31.885  1.00 34.58      AAAA O
ATOM   3392  N   LYS   359      44.387  55.188  31.461  1.00 36.00      AAAA N
ATOM   3394  CA  LYS   359      43.898  55.419  30.117  1.00 41.27      AAAA C
ATOM   3395  CB  LYS   359      44.845  54.707  29.174  1.00 37.40      AAAA C
ATOM   3396  CG  LYS   359      44.340  54.473  27.770  1.00 45.19      AAAA C
ATOM   3397  CD  LYS   359      45.040  55.317  26.750  1.00 43.40      AAAA C
ATOM   3398  CE  LYS   359      45.958  54.402  25.986  1.00 43.56      AAAA C
ATOM   3399  NZ  LYS   359      45.416  53.937  24.680  1.00 47.98      AAAA N
ATOM   3403  C   LYS   359      42.423  54.979  29.939  1.00 42.14      AAAA C
ATOM   3404  O   LYS   359      42.056  53.791  30.006  1.00 40.40      AAAA O
ATOM   3405  N   ILE   360      41.602  55.974  29.572  1.00 37.16      AAAA N
ATOM   3407  CA  ILE   360      40.164  55.742  29.334  1.00 40.02      AAAA C
ATOM   3408  CB  ILE   360      39.297  56.804  30.048  1.00 38.10      AAAA C
ATOM   3409  CG2 ILE   360      37.887  56.277  29.932  1.00 39.42      AAAA C
ATOM   3410  CG1 ILE   360      39.769  57.111  31.481  1.00 28.54      AAAA C
ATOM   3411  CD1 ILE   360      39.423  56.037  32.491  1.00 33.16      AAAA C
ATOM   3412  C   ILE   360      39.888  55.837  27.834  1.00 39.49      AAAA C
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ATOM   3413  O   ILE   360      40.014  56.942  27.235  1.00 37.32      AAAA O
ATOM   3414  N   ARG   361      39.567  54.721  27.221  1.00 34.34      AAAA N
ATOM   3416  CA  ARG   361      39.472  54.782  25.744  1.00 41.24      AAAA C
ATOM   3417  CB  ARG   361      40.783  54.213  25.148  1.00 47.92      AAAA C
ATOM   3418  CG  ARG   361      40.805  54.203  23.646  1.00 50.39      AAAA C
ATOM   3419  CD  ARG   361      41.943  53.357  23.116  1.00 51.36      AAAA C
ATOM   3420  NE  ARG   361      41.473  51.974  23.263  1.00 50.97      AAAA N
ATOM   3422  CZ  ARG   361      42.297  50.962  23.490  1.00 55.78      AAAA C
ATOM   3423  NH1 ARG   361      43.612  51.074  23.616  1.00 51.62      AAAA N
ATOM   3426  NH2 ARG   361      41.834  49.719  23.631  1.00 54.52      AAAA N
ATOM   3429  C   ARG   361      38.382  53.866  25.246  1.00 42.06      AAAA C
ATOM   3430  O   ARG   361      38.336  52.661  25.499  1.00 38.93      AAAA O
ATOM   3431  N   HIS   362      37.514  54.342  24.373  1.00 46.19      AAAA N
ATOM   3433  CA  HIS   362      36.372  53.555  23.885  1.00 49.34      AAAA C
ATOM   3434  CB  HIS   362      37.000  52.300  23.266  1.00 40.94      AAAA C
ATOM   3435  CG  HIS   362      37.849  52.610  22.084  1.00 42.78      AAAA C
ATOM   3436  CD2 HIS   362      38.049  53.765  21.411  1.00 48.32      AAAA C
ATOM   3437  ND1 HIS   362      38.628  51.676  21.469  1.00 43.59      AAAA N
ATOM   3439  CE1 HIS   362      39.256  52.247  20.465  1.00 46.01      AAAA C
ATOM   3440  NE2 HIS   362      38.923  53.515  20.408  1.00 49.22      AAAA N
ATOM   3442  C   HIS   362      35.295  53.113  24.913  1.00 50.32      AAAA C
ATOM   3443  O   HIS   362      34.686  52.030  24.795  1.00 41.31      AAAA O
ATOM   3444  N   SER   363      35.222  53.875  26.013  1.00 46.96      AAAA N
ATOM   3446  CA  SER   363      34.402  53.456  27.139  1.00 52.19      AAAA C
ATOM   3447  CB  SER   363      35.231  53.837  28.400  1.00 53.73      AAAA C
ATOM   3448  OG  SER   363      35.713  52.558  28.816  1.00 41.72      AAAA O
ATOM   3450  C   SER   363      33.005  54.072  27.046  1.00 49.08      AAAA C
ATOM   3451  O   SER   363      32.653  55.040  27.694  1.00 37.49      AAAA O
ATOM   3452  N   HIS   364      32.243  53.577  26.058  1.00 52.25      AAAA N
ATOM   3454  CA  HIS   364      30.954  54.173  25.717  1.00 53.66      AAAA C
ATOM   3455  C   HIS   364      29.879  53.937  26.760  1.00 48.77      AAAA C
ATOM   3456  O   HIS   364      29.297  54.899  27.280  1.00 51.44      AAAA O
ATOM   3457  CB  HIS   364      30.485  53.699  24.348  1.00 49.83      AAAA C
ATOM   3458  CG  HIS   364      31.493  54.182  23.338  1.00 51.51      AAAA C
ATOM   3459  ND1 HIS   364      31.870  55.502  23.156  1.00 44.83      AAAA N
ATOM   3460  CE1 HIS   364      32.798  55.533  22.214  1.00 28.57      AAAA C
ATOM   3461  CD2 HIS   364      32.194  53.393  22.472  1.00 38.62      AAAA C
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ATOM   3466  CA  ALA   365      29.211  52.488  28.621  1.00 44.41      AAAA C
ATOM   3467  CB  ALA   365      29.678  51.133  29.150  1.00 40.28      AAAA C
ATOM   3468  C   ALA   365      29.318  53.473  29.768  1.00 44.70      AAAA C
ATOM   3469  O   ALA   365      28.576  53.206  30.726  1.00 45.28      AAAA O
ATOM   3470  N   LEU   366      30.158  54.517  29.762  1.00 40.80      AAAA N
ATOM   3472  CA  LEU   366      30.415  55.243  30.968  1.00 42.21      AAAA C
ATOM   3473  CB  LEU   366      31.885  55.241  31.350  1.00 43.78      AAAA C
ATOM   3474  CG  LEU   366      32.740  54.037  31.667  1.00 51.52      AAAA C
ATOM   3475  CD1 LEU   366      34.192  54.373  32.043  1.00 51.77      AAAA C
ATOM   3476  CD2 LEU   366      32.118  53.305  32.834  1.00 51.17      AAAA C
ATOM   3477  C   LEU   366      29.974  56.687  30.896  1.00 46.36      AAAA C
ATOM   3478  O   LEU   366      30.305  57.248  29.849  1.00 48.40      AAAA O
ATOM   3479  N   VAL   367      29.521  57.275  32.015  1.00 43.68      AAAA N
ATOM   3481  CA  VAL   367      29.072  58.675  31.940  1.00 44.18      AAAA C
ATOM   3482  CB  VAL   367      27.557  58.727  32.376  1.00 48.80      AAAA C
ATOM   3483  CG1 VAL   367      26.923  60.073  32.571  1.00 41.69      AAAA C
ATOM   3484  CG2 VAL   367      26.697  57.949  31.365  1.00 34.00      AAAA C
ATOM   3485  C   VAL   367      29.923  59.518  32.845  1.00 44.90      AAAA C
ATOM   3486  O   VAL   367      29.965  60.751  32.720  1.00 44.75      AAAA O
ATOM   3487  N   SER   368      30.591  58.818  33.757  1.00 48.72      AAAA N
ATOM   3489  CA  SER   368      31.487  59.465  34.742  1.00 52.70      AAAA C
ATOM   3490  CB  SER   368      30.658  59.706  36.000  1.00 55.32      AAAA C
ATOM   3491  OG  SER   368      31.300  60.298  37.091  1.00 64.86      AAAA O
ATOM   3493  C   SER   368      32.590  58.497  35.179  1.00 52.76      AAAA C
ATOM   3494  O   SER   368      32.352  57.299  34.976  1.00 48.99      AAAA O
ATOM   3495  N   LEU   369      33.631  59.012  35.831  1.00 53.86      AAAA N
ATOM   3497  CA  LEU   369      34.716  58.129  36.274  1.00 60.15      AAAA C
ATOM   3498  CB  LEU   369      36.073  58.630  35.784  1.00 55.91      AAAA C
ATOM   3499  CG  LEU   369      36.325  58.736  34.271  1.00 45.96      AAAA C
ATOM   3500  CD1 LEU   369      37.669  59.428  34.154  1.00 53.97      AAAA C
ATOM   3501  CD2 LEU   369      36.207  57.384  33.619  1.00 38.77      AAAA C
ATOM   3502  C   LEU   369      34.645  58.036  37.811  1.00 62.52      AAAA C
ATOM   3503  O   LEU   369      35.569  57.700  38.595  1.00 59.33      AAAA O
ATOM   3504  N   SER   370      33.437  58.401  38.285  1.00 56.26      AAAA N
ATOM   3506  CA  SER   370      33.089  58.431  39.690  1.00 53.88      AAAA C
ATOM   3507  CB  SER   370      31.673  59.052  39.816  1.00 57.50      AAAA C
ATOM   3508  OG  SER   370      30.771  58.061  39.261  1.00 69.12      AAAA O
ATOM   3510  C   SER   370      33.060  57.085  40.412  1.00 47.97      AAAA C
ATOM   3511  O   SER   370      33.228  56.943  41.596  1.00 41.93      AAAA O
ATOM   3512  N   PHE   371      32.967  55.936  39.792  1.00 45.48      AAAA N
ATOM   3514  CA  PHE   371      33.223  54.643  40.356  1.00 46.29      AAAA C
ATOM   3515  CB  PHE   371      32.952  53.596  39.287  1.00 43.53      AAAA C
ATOM   3516  CG  PHE   371      33.724  53.629  38.012  1.00 56.45      AAAA C
ATOM   3517  CD1 PHE   371      34.805  52.807  37.764  1.00 58.95      AAAA C
ATOM   3518  CD2 PHE   371      33.371  54.515  37.004  1.00 53.92      AAAA C
ATOM   3519  CE1 PHE   371      35.498  52.842  36.570  1.00 59.50      AAAA C
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ATOM   3520  CE2 PHE   371      34.048  54.546  35.817  1.00 56.49      AAAA C
ATOM   3521  CZ  PHE   371      35.119  53.716  35.579  1.00 56.39      AAAA C
ATOM   3522  C   PHE   371      34.654  54.467  40.895  1.00 54.84      AAAA C
ATOM   3523  O   PHE   371      35.005  53.592  41.728  1.00 52.23      AAAA O
ATOM   3524  N   LEU   372      35.633  55.305  40.510  1.00 50.17      AAAA N
ATOM   3526  CA  LEU   372      36.928  55.395  41.109  1.00 46.25      AAAA C
ATOM   3527  CB  LEU   372      38.171  55.812  40.276  1.00 44.82      AAAA C
ATOM   3528  CG  LEU   372      38.411  54.800  39.114  1.00 36.78      AAAA C
ATOM   3529  CD1 LEU   372      38.853  55.643  37.934  1.00 45.04      AAAA C
ATOM   3530  CD2 LEU   372      39.260  53.657  39.565  1.00 35.55      AAAA C
ATOM   3531  C   LEU   372      36.715  56.392  42.243  1.00 42.26      AAAA C
ATOM   3532  O   LEU   372      37.224  57.507  42.364  1.00 38.37      AAAA O
ATOM   3533  N   LYS   373      35.970  55.862  43.192  1.00 47.06      AAAA N
ATOM   3535  CA  LYS   373      35.527  56.509  44.415  1.00 50.19      AAAA C
ATOM   3536  CB  LYS   373      34.546  55.521  45.077  1.00 56.74      AAAA C
ATOM   3537  CG  LYS   373      33.645  56.162  46.119  1.00 59.64      AAAA C
ATOM   3538  CD  LYS   373      32.529  56.955  45.441  0.01 60.17      AAAA C
ATOM   3539  CE  LYS   373      31.674  57.687  46.460  0.01 60.45      AAAA C
ATOM   3540  NZ  LYS   373      31.083  58.933  45.899  0.01 60.38      AAAA N
ATOM   3544  C   LYS   373      36.646  56.863  45.366  1.00 49.72      AAAA C
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ATOM   3549  CB  ASN   374      39.080  55.154  47.314  1.00 63.16      AAAA C
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ATOM   3552  ND2 ASN   374      37.160  55.965  48.578  1.00 52.88      AAAA N
ATOM   3555  C   ASN   374      40.043  56.892  45.786  1.00 62.35      AAAA C
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ATOM   3560  CB  LEU   375      41.099  57.359  42.288  1.00 56.41      AAAA C
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ATOM   3563  CD2 LEU   375      42.030  57.796  40.041  1.00 40.97      AAAA C
ATOM   3564  C   LEU   375      41.712  58.754  44.245  1.00 52.37      AAAA C
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ATOM   3566  N   ARG   376      42.801  58.874  44.982  1.00 55.16      AAAA N
ATOM   3568  CA  ARG   376      43.320  60.155  45.434  1.00 55.45      AAAA C
ATOM   3569  CB  ARG   376      43.706  60.222  46.928  1.00 58.68      AAAA C
ATOM   3570  CG  ARG   376      44.288  58.907  47.415  1.00 69.10      AAAA C
ATOM   3571  CD  ARG   376      44.286  58.817  48.944  1.00 81.17      AAAA C
ATOM   3572  NE  ARG   376      45.377  57.926  49.410  1.00 84.46      AAAA N
ATOM   3574  CZ  ARG   376      46.618  58.380  49.598  1.00 85.64      AAAA C
ATOM   3575  NH1 ARG   376      46.966  59.645  49.383  1.00 81.84      AAAA N
ATOM   3578  NH2 ARG   376      47.571  57.548  50.012  1.00 94.15      AAAA N
ATOM   3581  C   ARG   376      44.556  60.544  44.633  1.00 50.16      AAAA C
ATOM   3582  O   ARG   376      44.746  61.728  44.465  1.00 44.25      AAAA O
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ATOM   3586  CB  LEU   377      47.596  60.411  44.329  1.00 64.72      AAAA C
ATOM   3587  CG  LEU   377      48.806  59.577  44.667  1.00 70.76      AAAA C
ATOM   3588  CD1 LEU   377      50.031  60.157  43.954  1.00 63.32      AAAA C
ATOM   3589  CD2 LEU   377      49.010  59.696  46.179  1.00 68.60      AAAA C
ATOM   3590  C   LEU   377      47.043  59.022  42.311  1.00 46.33      AAAA C
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ATOM   3595  CB  ILE   378      47.342  59.303  38.724  1.00 46.36      AAAA C
ATOM   3596  CG2 ILE   378      48.115  58.696  37.574  1.00 34.36      AAAA C
ATOM   3597  CG1 ILE   378      45.871  58.862  38.829  1.00 38.59      AAAA C
ATOM   3598  CD1 ILE   378      44.999  59.515  37.765  1.00 37.18      AAAA C
ATOM   3599  C   ILE   378      49.524  59.381  40.003  1.00 49.87      AAAA C
ATOM   3600  O   ILE   378      49.801  60.595  40.040  1.00 44.72      AAAA O
ATOM   3601  N   LEU   379      50.454  58.423  40.067  1.00 49.97      AAAA N
ATOM   3603  CA  LEU   379      51.866  58.712  40.344  1.00 48.48      AAAA C
ATOM   3604  CB  LEU   379      52.575  57.531  41.054  1.00 48.44      AAAA C
ATOM   3605  CG  LEU   379      52.234  57.363  42.554  1.00 50.28      AAAA C
ATOM   3606  CD1 LEU   379      52.926  56.187  43.217  1.00 39.89      AAAA C
ATOM   3607  CD2 LEU   379      52.616  58.625  43.300  1.00 42.89      AAAA C
ATOM   3608  C   LEU   379      52.609  59.019  39.080  1.00 50.94      AAAA C
ATOM   3609  O   LEU   379      53.576  59.788  39.139  1.00 54.23      AAAA O
ATOM   3610  N   GLY   380      52.175  58.423  37.972  1.00 48.67      AAAA N
ATOM   3612  CA  GLY   380      52.931  58.715  36.702  1.00 49.94      AAAA C
ATOM   3613  C   GLY   380      54.249  58.155  36.624  1.00 52.70      AAAA C
ATOM   3614  O   GLY   380      55.026  58.657  35.803  1.00 49.94      AAAA O
ATOM   3615  N   GLU   381      54.549  57.033  37.272  1.00 52.51      AAAA N
ATOM   3617  CA  GLU   381      55.849  56.386  37.243  1.00 52.33      AAAA C
ATOM   3618  CB  GLU   381      56.055  55.310  38.323  1.00 45.22      AAAA C
ATOM   3619  CG  GLU   381      55.402  55.779  39.636  1.00 52.91      AAAA C
ATOM   3620  CD  GLU   381      56.050  55.192  40.873  1.00 42.11      AAAA C
ATOM   3621  OE1 GLU   381      56.160  53.966  40.890  1.00 40.26      AAAA O
ATOM   3622  OE2 GLU   381      56.379  56.014  41.754  1.00 51.32      AAAA O
ATOM   3623  C   GLU   381      56.078  55.784  35.859  1.00 55.86      AAAA C
ATOM   3624  O   GLU   381      57.216  55.652  35.345  1.00 54.61      AAAA O
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ATOM   3625  N   GLU   382      54.980  55.449  35.157  1.00 53.56      AAAA N
ATOM   3627  CA  GLU   382      55.091  55.018  33.766  1.00 48.15      AAAA C
ATOM   3628  CB  GLU   382      55.051  53.550  33.532  1.00 35.27      AAAA C
ATOM   3629  CG  GLU   382      54.739  53.225  32.051  1.00 49.69      AAAA C
ATOM   3630  CD  GLU   382      54.676  51.719  31.807  1.00 56.45      AAAA C
ATOM   3631  OE1 GLU   382      55.062  50.924  32.705  1.00 61.66      AAAA O
ATOM   3632  OE2 GLU   382      54.264  51.201  30.745  1.00 57.69      AAAA O
ATOM   3633  C   GLU   382      54.006  55.732  32.973  1.00 50.84      AAAA C
ATOM   3634  O   GLU   382      53.097  56.282  33.598  1.00 49.44      AAAA O
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ATOM   3637  CA  GLN   383      53.498  57.153  31.016  1.00 40.15      AAAA C
ATOM   3638  CB  GLN   383      53.914  58.609  31.155  1.00 28.50      AAAA C
ATOM   3639  CG  GLN   383      54.489  58.909  32.542  1.00 31.10      AAAA C
ATOM   3640  CD  GLN   383      54.950  60.301  32.752  1.00 33.19      AAAA C
ATOM   3641  OE1 GLN   383      55.186  60.840  31.683  1.00 40.34      AAAA O
ATOM   3642  NE2 GLN   383      55.043  60.943  33.934  1.00 36.30      AAAA N
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ATOM   3646  O   GLN   383      54.131  55.858  29.139  1.00 43.45      AAAA O
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ATOM   3649  CA  LEU   384      52.257  56.889  27.443  1.00 43.24      AAAA C
ATOM   3650  CB  LEU   384      50.814  57.011  26.949  1.00 43.79      AAAA C
ATOM   3651  CG  LEU   384      49.818  56.235  27.861  1.00 41.21      AAAA C
ATOM   3652  CD1 LEU   384      48.611  57.095  28.221  1.00 33.99      AAAA C
ATOM   3653  CD2 LEU   384      49.405  54.968  27.149  1.00 33.20      AAAA C
ATOM   3654  C   LEU   384      53.204  57.809  26.672  1.00 40.51      AAAA C
ATOM   3655  O   LEU   384      53.582  58.872  27.177  1.00 29.66      AAAA O
ATOM   3656  N   GLU   385      53.659  57.319  25.531  1.00 45.22      AAAA N
ATOM   3658  CA  GLU   385      54.410  58.116  24.570  1.00 49.98      AAAA C
ATOM   3659  CB  GLU   385      54.424  57.475  23.174  1.00 60.50      AAAA C
ATOM   3660  CG  GLU   385      55.045  56.095  23.106  1.00 68.76      AAAA C
ATOM   3661  CD  GLU   385      54.195  54.951  23.592  1.00 72.07      AAAA C
ATOM   3662  OE1 GLU   385      53.150  55.213  24.244  1.00 81.88      AAAA O
ATOM   3663  OE2 GLU   385      54.565  53.786  23.301  1.00 73.13      AAAA O
ATOM   3664  C   GLU   385      53.828  59.515  24.450  1.00 47.41      AAAA C
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ATOM   3666  N   GLY   386      54.614  60.470  24.902  1.00 43.69      AAAA N
ATOM   3668  CA  GLY   386      54.181  61.870  24.897  1.00 40.34      AAAA C
ATOM   3669  C   GLY   386      54.286  62.449  26.308  1.00 40.65      AAAA C
ATOM   3670  O   GLY   386      53.930  63.615  26.491  1.00 39.75      AAAA O
ATOM   3671  N   ASN   387      54.441  61.537  27.272  1.00 40.75      AAAA N
ATOM   3673  CA  ASN   387      54.479  61.912  28.675  1.00 49.18      AAAA C
ATOM   3674  CB  ASN   387      55.500  63.084  28.874  1.00 44.41      AAAA C
ATOM   3675  CG  ASN   387      56.925  62.541  28.722  1.00 61.51      AAAA C
ATOM   3676  OD1 ASN   387      57.199  61.313  28.677  1.00 57.85      AAAA O
ATOM   3677  ND2 ASN   387      58.063  63.251  28.592  1.00 61.96      AAAA N
ATOM   3680  C   ASN   387      53.095  62.100  29.299  1.00 48.46      AAAA C
ATOM   3681  O   ASN   387      52.836  62.891  30.218  1.00 48.99      AAAA O
ATOM   3682  N   TYR   388      52.214  61.116  29.058  1.00 46.29      AAAA N
ATOM   3684  CA  TYR   388      50.846  61.199  29.540  1.00 45.09      AAAA C
ATOM   3685  CB  TYR   388      49.823  60.957  28.399  1.00 40.70      AAAA C
ATOM   3686  CG  TYR   388      49.925  62.056  27.373  1.00 42.24      AAAA C
ATOM   3687  CD1 TYR   388      50.343  61.854  26.064  1.00 44.38      AAAA C
ATOM   3688  CE1 TYR   388      50.401  62.885  25.157  1.00 35.51      AAAA C
ATOM   3689  CD2 TYR   388      49.625  63.356  27.709  1.00 44.67      AAAA C
ATOM   3690  CE2 TYR   388      49.699  64.428  26.830  1.00 38.14      AAAA C
ATOM   3691  CZ  TYR   388      50.087  64.148  25.555  1.00 41.27      AAAA C
ATOM   3692  OH  TYR   388      50.151  65.181  24.604  1.00 50.18      AAAA O
ATOM   3694  C   TYR   388      50.563  60.288  30.714  1.00 41.88      AAAA C
ATOM   3695  O   TYR   388      50.727  59.092  30.511  1.00 32.99      AAAA O
ATOM   3696  N   SER   389      50.020  60.917  31.763  1.00 45.42      AAAA N
ATOM   3698  CA  SER   389      49.591  60.131  32.931  1.00 50.13      AAAA C
ATOM   3699  CB  SER   389      49.798  60.894  34.261  1.00 45.57      AAAA C
ATOM   3700  OG  SER   389      51.185  60.899  34.504  1.00 51.11      AAAA O
ATOM   3702  C   SER   389      48.097  59.813  32.804  1.00 48.11      AAAA C
ATOM   3703  O   SER   389      47.686  58.792  33.336  1.00 49.25      AAAA O
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ATOM   3706  CA  PHE   390      45.867  60.595  32.146  1.00 40.76      AAAA C
ATOM   3707  CB  PHE   390      45.241  61.581  33.139  1.00 44.80      AAAA C
ATOM   3708  CG  PHE   390      43.764  61.358  33.328  1.00 40.53      AAAA C
ATOM   3709  CD1 PHE   390      43.406  60.273  34.089  1.00 40.80      AAAA C
ATOM   3710  CD2 PHE   390      42.768  62.157  32.748  1.00 35.59      AAAA C
ATOM   3711  CE1 PHE   390      42.050  59.985  34.312  1.00 47.09      AAAA C
ATOM   3712  CE2 PHE   390      41.454  61.824  32.965  1.00 44.50      AAAA C
ATOM   3713  CZ  PHE   390      41.063  60.745  33.739  1.00 34.54      AAAA C
ATOM   3714  C   PHE   390      45.372  60.829  30.720  1.00 38.54      AAAA C
ATOM   3715  O   PHE   390      45.542  61.918  30.126  1.00 40.29      AAAA O
ATOM   3716  N   TYR   391      44.819  59.818  30.096  1.00 33.48      AAAA N
ATOM   3718  CA  TYR   391      44.596  59.782  28.663  1.00 38.58      AAAA C
ATOM   3719  CB  TYR   391      45.579  58.871  27.972  1.00 38.95      AAAA C
ATOM   3720  CG  TYR   391      45.760  59.006  26.503  1.00 44.54      AAAA C
ATOM   3721  CD1 TYR   391      46.822  59.815  26.052  1.00 47.14      AAAA C
ATOM   3722  CE1 TYR   391      47.057  59.993  24.722  1.00 46.03      AAAA C
ATOM   3723  CD2 TYR   391      44.927  58.390  25.584  1.00 46.94      AAAA C
ATOM   3724  CE2 TYR   391      45.157  58.560  24.242  1.00 47.45      AAAA C
ATOM   3725  CZ  TYR   391      46.207  59.350  23.830  1.00 45.84      AAAA C
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ATOM   3726  OH  TYR   391      46.374  59.492  22.481  1.00 44.70      AAAA O
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ATOM   3729  O   TYR   391      42.841  58.103  28.730  1.00 38.49      AAAA O
ATOM   3730  N   VAL   392      42.417  60.158  27.779  1.00 37.07      AAAA N
ATOM   3732  CA  VAL   392      40.958  59.874  27.603  1.00 39.52      AAAA C
ATOM   3733  CB  VAL   392      40.075  60.880  28.440  1.00 41.12      AAAA C
ATOM   3734  CG1 VAL   392      38.612  60.464  28.472  1.00 37.96      AAAA C
ATOM   3735  CG2 VAL   392      40.666  61.041  29.841  1.00 33.19      AAAA C
ATOM   3736  C   VAL   392      40.531  60.092  26.182  1.00 31.08      AAAA C
ATOM   3737  O   VAL   392      40.508  61.277  25.804  1.00 34.71      AAAA O
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ATOM   3741  CB  LEU   393      41.200  59.036  23.096  1.00 42.49      AAAA C
ATOM   3742  CG  LEU   393      41.023  58.649  21.586  1.00 26.48      AAAA C
ATOM   3743  CD1 LEU   393      41.128  59.879  20.753  1.00 26.57      AAAA C
ATOM   3744  CD2 LEU   393      42.078  57.589  21.244  1.00 29.98      AAAA C
ATOM   3745  C   LEU   393      38.821  58.375  23.482  1.00 39.15      AAAA C
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ATOM   3752  OD1 ASP   394      36.750  55.577  19.333  1.00 52.91      AAAA O
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ATOM   3755  O   ASP   394      35.831  56.385  23.212  1.00 43.51      AAAA O
ATOM   3756  N   ASN   395      35.299  58.495  23.746  1.00 39.90      AAAA N
ATOM   3758  CA  ASN   395      34.305  58.158  24.776  1.00 46.32      AAAA C
ATOM   3759  CB  ASN   395      34.804  58.512  26.212  1.00 42.96      AAAA C
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ATOM   3761  OD1 ASN   395      36.013  56.394  26.796  1.00 21.65      AAAA O
ATOM   3762  ND2 ASN   395      37.075  58.409  26.559  1.00 27.87      AAAA N
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ATOM   3766  O   ASN   395      32.749  59.982  24.882  1.00 37.06      AAAA O
ATOM   3767  N   GLN   396      32.073  58.055  23.877  1.00 46.74      AAAA N
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ATOM   3771  CG  GLN   396      30.173  57.405  21.257  1.00 46.42      AAAA C
ATOM   3772  CD  GLN   396      29.817  55.991  20.840  1.00 55.21      AAAA C
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ATOM   3774  NE2 GLN   396      30.628  55.411  19.971  1.00 55.79      AAAA N
ATOM   3777  C   GLN   396      29.874  59.224  24.458  1.00 48.64      AAAA C
ATOM   3778  O   GLN   396      29.407  60.287  24.113  1.00 51.63      AAAA O
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ATOM   3783  CG  ASN   397      27.231  57.430  25.860  1.00 49.09      AAAA C
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ATOM   3785  ND2 ASN   397      27.258  56.175  25.431  1.00 43.31      AAAA N
ATOM   3788  C   ASN   397      29.367  59.945  27.990  1.00 52.98      AAAA C
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ATOM   3794  CG  LEU   398      33.606  60.283  30.460  1.00 41.81      AAAA C
ATOM   3795  CD1 LEU   398      33.417  58.939  31.136  1.00 40.35      AAAA C
ATOM   3796  CD2 LEU   398      35.070  60.608  30.082  1.00 39.03      AAAA C
ATOM   3797  C   LEU   398      30.923  61.995  29.353  1.00 52.35      AAAA C
ATOM   3798  O   LEU   398      31.422  62.909  28.681  1.00 49.91      AAAA O
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ATOM   3802  CB  GLN   399      28.236  63.331  31.262  1.00 59.55      AAAA C
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ATOM   3814  CB  ASN   400      31.215  64.314  35.049  1.00 54.97      AAAA C
ATOM   3815  CG  ASN   400      30.717  63.150  35.897  1.00 58.99      AAAA C
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ATOM   3817  OE1 ASN   400      30.906  64.502  37.962  1.00 68.10      AAAA O
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ATOM   3821  C   GLN   400      33.113  63.008  34.052  1.00 52.08      AAAA C
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ATOM   3826  CB  LEU   401      36.378  63.803  35.260  1.00 47.94      AAAA C
ATOM   3827  CG  LEU   401      36.638  64.237  33.772  1.00 46.61      AAAA C
ATOM   3828  CD1 LEU   401      37.658  65.326  33.677  1.00 39.09      AAAA C
ATOM   3829  CD2 LEU   401      36.919  63.069  32.860  1.00 40.72      AAAA C
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ATOM   3835  CB  TRP   402      36.279  62.953  39.933  1.00 59.56      AAAA C
ATOM   3836  CG  TRP   402      36.971  61.624  39.737  1.00 58.17      AAAA C
ATOM   3837  CD2 TRP   402      37.981  61.243  38.784  1.00 53.18      AAAA C
ATOM   3838  CE2 TRP   402      38.286  59.897  39.002  1.00 56.61      AAAA C
ATOM   3839  CE3 TRP   402      38.643  61.917  37.764  1.00 43.25      AAAA C
ATOM   3840  CD1 TRP   402      36.719  60.517  40.459  1.00 53.50      AAAA C
ATOM   3841  NE1 TRP   402      37.488  59.467  40.032  1.00 57.66      AAAA N
ATOM   3843  CZ2 TRP   402      39.212  59.160  38.249  1.00 51.44      AAAA C
ATOM   3844  CZ3 TRP   402      39.546  61.199  37.026  1.00 53.69      AAAA C
ATOM   3845  CH2 TRP   402      39.820  59.857  37.263  1.00 50.75      AAAA C
ATOM   3846  C   TRP   402      34.223  64.389  39.429  1.00 64.09      AAAA C
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ATOM   3851  CB  ASP   403      31.918  65.343  42.151  1.00 72.19      AAAA C
ATOM   3852  CG  ASP   403      30.853  66.417  42.306  1.00 73.08      AAAA C
ATOM   3853  OD1 ASP   403      31.177  67.625  42.297  1.00 71.67      AAAA O
ATOM   3854  OD2 ASP   403      29.693  65.979  42.454  1.00 75.08      AAAA O
ATOM   3855  C   ASP   403      34.005  66.607  41.607  1.00 66.63      AAAA C
ATOM   3856  O   ASP   403      34.245  66.672  42.811  1.00 67.18      AAAA O
ATOM   3857  N   TRP   404      34.449  67.588  40.846  1.00 69.29      AAAA N
ATOM   3859  CA  TRP   404      35.412  68.588  41.291  1.00 77.11      AAAA C
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ATOM   3861  CG  TRP   404      36.504  68.509  39.047  1.00 82.59      AAAA C
ATOM   3862  CD2 TRP   404      37.294  67.346  39.322  1.00 84.82      AAAA C
ATOM   3863  CE2 TRP   404      37.686  66.813  38.081  1.00 84.56      AAAA C
ATOM   3864  CE3 TRP   404      37.703  66.710  40.506  1.00 80.95      AAAA C
ATOM   3865  CD1 TRP   404      36.460  68.622  37.694  1.00 83.37      AAAA C
ATOM   3866  NE1 TRP   404      37.165  67.617  37.111  1.00 80.33      AAAA N
ATOM   3868  CZ2 TRP   404      38.477  65.662  37.982  1.00 85.91      AAAA C
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ATOM   3870  CH2 TRP   404      38.860  65.051  39.133  1.00 85.05      AAAA C
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ATOM   3875  CA  ASP   405      33.771  69.861  44.496  1.00 87.48      AAAA C
ATOM   3876  CB  ASP   405      32.352  70.365  44.262  1.00 88.04      AAAA C
ATOM   3877  CG  ASP   405      32.274  71.612  43.409  1.00 92.54      AAAA C
ATOM   3878  OD1 ASP   405      33.306  72.285  43.207  1.00 94.82      AAAA O
ATOM   3879  OD2 ASP   405      31.130  71.854  42.955  1.00 95.26      AAAA O
ATOM   3880  C   ASP   405      33.730  68.906  45.693  1.00 87.80      AAAA C
ATOM   3881  O   ASP   405      34.245  69.224  46.743  1.00 92.18      AAAA O
ATOM   3882  N   ALA   406      33.239  67.709  45.460  1.00 84.46      AAAA N
ATOM   3884  CA  ALA   406      33.176  66.671  46.451  1.00 82.87      AAAA C
ATOM   3885  CB  ALA   406      31.943  65.805  46.133  1.00 76.32      AAAA C
ATOM   3886  C   ALA   406      34.445  65.840  46.459  1.00 85.77      AAAA C
ATOM   3887  O   ALA   406      34.470  64.823  47.185  1.00 89.38      AAAA O
ATOM   3888  N   ARG   407      35.433  66.073  45.577  1.00 83.74      AAAA N
ATOM   3890  CA  ARG   407      36.541  65.151  45.400  1.00 79.60      AAAA C
ATOM   3891  CB  ARG   407      36.165  64.140  44.297  1.00 77.84      AAAA C
ATOM   3892  CG  ARG   407      35.457  62.950  44.921  1.00 81.91      AAAA C
ATOM   3893  CD  ARG   407      35.362  61.688  44.113  1.00 86.97      AAAA C
ATOM   3894  NE  ARG   407      36.281  60.660  44.607  1.00 86.94      AAAA N
ATOM   3896  CZ  ARG   407      37.564  60.583  44.279  1.00 92.14      AAAA C
ATOM   3897  NH1 ARG   407      38.169  61.441  43.469  1.00 97.06      AAAA N
ATOM   3900  NH2 ARG   407      38.309  59.616  44.770  1.00 96.33      AAAA N
ATOM   3903  C   ARG   407      37.880  65.749  45.048  1.00 76.72      AAAA C
ATOM   3904  O   ARG   407      37.989  66.774  44.410  1.00 77.47      AAAA O
ATOM   3905  N   ASN   408      38.958  65.081  45.453  1.00 75.75      AAAA N
ATOM   3907  CA  ASN   408      40.311  65.556  45.173  1.00 73.79      AAAA C
ATOM   3908  CB  ASN   408      40.938  66.240  46.388  1.00 74.46      AAAA C
ATOM   3909  CG  ASN   408      41.986  67.242  45.947  1.00 82.51      AAAA C
ATOM   3910  OD1 ASN   408      41.813  68.429  46.240  1.00 90.33      AAAA O
ATOM   3911  ND2 ASN   408      43.028  66.821  45.253  1.00 84.46      AAAA N
ATOM   3914  C   ASN   408      41.257  64.468  44.654  1.00 65.97      AAAA C
ATOM   3915  O   ASN   408      41.251  63.374  45.151  1.00 63.82      AAAA O
ATOM   3916  N   LEU   409      42.041  64.793  43.650  1.00 61.41      AAAA N
ATOM   3918  CA  LEU   409      42.896  63.872  42.947  1.00 60.90      AAAA C
ATOM   3919  CB  LEU   409      42.153  63.250  41.768  1.00 62.98      AAAA C
ATOM   3920  CG  LEU   409      42.992  62.553  40.704  1.00 59.77      AAAA C
ATOM   3921  CD1 LEU   409      43.488  61.205  41.197  1.00 54.06      AAAA C
ATOM   3922  CD2 LEU   409      42.094  62.445  39.486  1.00 55.74      AAAA C
ATOM   3923  C   LEU   409      44.151  64.599  42.485  1.00 61.19      AAAA C
ATOM   3924  O   LEU   409      44.141  65.809  42.370  1.00 60.64      AAAA O
ATOM   3925  N   THR   410      45.281  63.903  42.424  1.00 63.74      AAAA N
ATOM   3927  CA  THR   410      46.588  64.462  42.131  1.00 60.44      AAAA C
ATOM   3928  CB  THR   410      47.454  64.676  43.385  1.00 67.08      AAAA C
ATOM   3929  OG1 THR   410      46.870  65.746  44.157  1.00 74.29      AAAA O
ATOM   3931  CG2 THR   410      48.909  65.103  43.162  1.00 48.56      AAAA C
ATOM   3932  C   THR   410      47.426  63.565  41.218  1.00 56.62      AAAA C
ATOM   3933  O   THR   410      47.382  62.354  41.317  1.00 54.99      AAAA O
ATOM   3934  N   ILE   411      48.077  64.245  40.288  1.00 53.97      AAAA N
ATOM   3936  CA  ILE   411      48.897  63.562  39.291  1.00 53.29      AAAA C
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ATOM   3937  CB  ILE   411      48.409  63.854  37.864  1.00 49.81      AAAA C
ATOM   3938  CG2 ILE   411      49.216  63.128  36.806  1.00 30.86      AAAA C
ATOM   3939  CG1 ILE   411      46.911  63.489  37.729  1.00 40.83      AAAA C
ATOM   3940  CD1 ILE   411      46.322  63.547  36.338  1.00 38.51      AAAA C
ATOM   3941  C   ILE   411      50.319  64.018  39.568  1.00 55.38      AAAA C
ATOM   3942  O   ILE   411      50.656  65.179  39.291  1.00 57.59      AAAA O
ATOM   3943  N   SER   412      51.073  63.182  40.270  1.00 54.26      AAAA N
ATOM   3945  CA  SER   412      52.434  63.502  40.689  1.00 54.46      AAAA C
ATOM   3946  CB  SER   412      53.071  62.210  41.248  1.00 55.78      AAAA C
ATOM   3947  OG  SER   412      53.756  62.536  42.434  1.00 67.12      AAAA O
ATOM   3949  C   SER   412      53.326  63.910  39.523  1.00 55.52      AAAA C
ATOM   3950  O   SER   412      54.081  64.876  39.527  1.00 55.04      AAAA O
ATOM   3951  N   ALA   413      53.254  63.124  38.438  1.00 50.12      AAAA N
ATOM   3953  CA  ALA   413      54.064  63.402  37.281  1.00 50.01      AAAA C
ATOM   3954  CB  ALA   413      55.334  62.520  37.365  1.00 34.96      AAAA C
ATOM   3955  C   ALA   413      53.301  63.078  35.994  1.00 48.71      AAAA C
ATOM   3956  O   ALA   413      52.495  62.168  35.998  1.00 48.81      AAAA O
ATOM   3957  N   GLY   414      53.675  63.690  34.895  1.00 47.92      AAAA N
ATOM   3959  CA  GLY   414      53.057  63.454  33.607  1.00 51.75      AAAA C
ATOM   3960  C   GLY   414      52.017  64.524  33.294  1.00 52.77      AAAA C
ATOM   3961  O   GLY   414      51.684  65.370  34.114  1.00 53.23      AAAA O
ATOM   3962  N   LYS   415      51.385  64.406  32.138  1.00 56.31      AAAA N
ATOM   3964  CA  LYS   415      50.289  65.317  31.759  1.00 52.49      AAAA C
ATOM   3965  CB  LYS   415      50.884  66.358  30.833  1.00 50.94      AAAA C
ATOM   3966  CG  LYS   415      51.198  65.855  29.429  1.00 54.39      AAAA C
ATOM   3967  CD  LYS   415      52.288  66.691  28.765  1.00 53.96      AAAA C
ATOM   3968  CE  LYS   415      52.785  66.151  27.441  1.00 56.01      AAAA C
ATOM   3969  NZ  LYS   415      52.426  67.032  26.284  1.00 66.36      AAAA N
ATOM   3973  C   LYS   415      49.110  64.576  31.155  1.00 50.04      AAAA C
ATOM   3974  O   LYS   415      49.077  63.337  31.036  1.00 49.77      AAAA O
ATOM   3975  N   MET   416      48.091  65.353  30.771  1.00 48.34      AAAA N
ATOM   3977  CA  MET   416      46.890  64.734  30.186  1.00 46.77      AAAA C
ATOM   3978  CB  MET   416      45.629  65.186  30.949  1.00 42.79      AAAA C
ATOM   3979  CG  MET   416      45.836  65.880  32.273  1.00 40.91      AAAA C
ATOM   3980  SD  MET   416      44.511  65.636  33.517  1.00 56.20      AAAA S
ATOM   3981  CE  MET   416      44.002  67.366  33.690  1.00 35.94      AAAA C
ATOM   3982  C   MET   416      46.623  65.064  28.728  1.00 40.40      AAAA C
ATOM   3983  O   MET   416      46.963  66.137  28.247  1.00 34.84      AAAA O
ATOM   3984  N   TYR   417      45.893  64.169  28.104  1.00 38.49      AAAA N
ATOM   3986  CA  TYR   417      45.355  64.387  26.765  1.00 39.50      AAAA C
ATOM   3987  CB  TYR   417      46.156  63.471  25.831  1.00 32.02      AAAA C
ATOM   3988  CG  TYR   417      45.583  63.430  24.428  1.00 39.48      AAAA C
ATOM   3989  CD1 TYR   417      45.730  64.501  23.511  1.00 39.29      AAAA C
ATOM   3990  CE1 TYR   417      45.196  64.429  22.253  1.00 34.56      AAAA C
ATOM   3991  CD2 TYR   417      44.884  62.321  24.005  1.00 36.81      AAAA C
ATOM   3992  CE2 TYR   417      44.379  62.241  22.722  1.00 38.80      AAAA C
ATOM   3993  CZ  TYR   417      44.535  63.292  21.872  1.00 44.20      AAAA C
ATOM   3994  OH  TYR   417      44.053  63.361  20.552  1.00 58.10      AAAA O
ATOM   3996  C   TYR   417      43.853  64.065  26.698  1.00 44.18      AAAA C
ATOM   3997  O   TYR   417      43.376  62.974  27.135  1.00 42.19      AAAA O
ATOM   3998  N   PHE   418      43.068  64.971  26.100  1.00 45.84      AAAA N
ATOM   4000  CA  PHE   418      41.644  64.701  25.910  1.00 45.67      AAAA C
ATOM   4001  CB  PHE   418      40.772  65.657  26.730  1.00 47.19      AAAA C
ATOM   4002  CG  PHE   418      40.675  65.264  28.177  1.00 43.44      AAAA C
ATOM   4003  CD1 PHE   418      41.552  65.685  29.132  1.00 38.43      AAAA C
ATOM   4004  CD2 PHE   418      39.638  64.417  28.544  1.00 51.21      AAAA C
ATOM   4005  CE1 PHE   418      41.402  65.291  30.440  1.00 46.44      AAAA C
ATOM   4006  CE2 PHE   418      39.486  64.023  29.845  1.00 46.63      AAAA C
ATOM   4007  CZ  PHE   418      40.358  64.454  30.801  1.00 44.68      AAAA C
ATOM   4008  C   PHE   418      41.251  64.730  24.440  1.00 44.64      AAAA C
ATOM   4009  O   PHE   418      41.375  65.762  23.812  1.00 47.69      AAAA O
ATOM   4010  N   ALA   419      40.554  63.713  23.936  1.00 43.06      AAAA N
ATOM   4012  CA  ALA   419      40.015  63.793  22.607  1.00 39.21      AAAA C
ATOM   4013  CB  ALA   419      41.090  63.562  21.555  1.00 30.88      AAAA C
ATOM   4014  C   ALA   419      38.837  62.846  22.366  1.00 41.77      AAAA C
ATOM   4015  O   ALA   419      38.871  61.628  22.557  1.00 36.08      AAAA O
ATOM   4016  N   PHE   420      37.829  63.398  21.618  1.00 40.41      AAAA N
ATOM   4018  CA  PHE   420      36.742  62.621  21.070  1.00 40.03      AAAA C
ATOM   4019  CB  PHE   420      37.157  61.430  20.180  1.00 45.54      AAAA C
ATOM   4020  CG  PHE   420      37.832  61.909  18.912  1.00 54.18      AAAA C
ATOM   4021  CD1 PHE   420      39.221  61.987  18.751  1.00 49.23      AAAA C
ATOM   4022  CD2 PHE   420      37.006  62.345  17.871  1.00 47.65      AAAA C
ATOM   4023  CE1 PHE   420      39.783  62.496  17.567  1.00 46.00      AAAA C
ATOM   4024  CE2 PHE   420      37.572  62.833  16.725  1.00 51.10      AAAA C
ATOM   4025  CZ  PHE   420      38.964  62.928  16.549  1.00 44.01      AAAA C
ATOM   4026  C   PHE   420      35.762  62.146  22.136  1.00 41.65      AAAA C
ATOM   4027  O   PHE   420      35.352  60.991  22.215  1.00 38.35      AAAA O
ATOM   4028  N   ASN   421      35.459  63.024  23.049  1.00 45.35      AAAA N
ATOM   4030  CA  ASN   421      34.477  62.960  24.112  1.00 46.86      AAAA C
ATOM   4031  CB  ASN   421      35.183  63.276  25.449  1.00 43.60      AAAA C
ATOM   4032  CG  ASN   421      36.407  62.401  25.654  1.00 47.90      AAAA C
ATOM   4033  OD1 ASN   421      36.426  61.147  25.714  1.00 44.83      AAAA O
ATOM   4034  ND2 ASN   421      37.541  63.101  25.732  1.00 37.46      AAAA N
ATOM   4037  C   ASN   421      33.432  64.069  23.835  1.00 47.83      AAAA C
ATOM   4038  O   ASN   421      33.617  65.233  24.237  1.00 38.85      AAAA O
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ATOM   4039  N   PRO   422      32.453  63.777  22.968  1.00 47.86      AAAA N
ATOM   4040  CD  PRO   422      32.213  62.423  22.372  1.00 44.11      AAAA C
ATOM   4041  CA  PRO   422      31.463  64.776  22.605  1.00 47.85      AAAA C
ATOM   4042  CB  PRO   422      30.731  64.084  21.446  1.00 44.86      AAAA C
ATOM   4043  CG  PRO   422      30.947  62.623  21.606  1.00 43.01      AAAA C
ATOM   4044  C   PRO   422      30.577  65.284  23.735  1.00 51.16      AAAA C
ATOM   4045  O   PRO   422      30.223  66.486  23.744  1.00 48.54      AAAA O
ATOM   4046  N   LYS   423      30.320  64.487  24.774  1.00 52.90      AAAA N
ATOM   4048  CA  LYS   423      29.431  64.908  25.865  1.00 58.82      AAAA C
ATOM   4049  CB  LYS   423      28.556  63.721  26.360  1.00 52.93      AAAA C
ATOM   4050  CG  LYS   423      28.209  62.810  25.196  1.00 70.55      AAAA C
ATOM   4051  CD  LYS   423      26.743  62.448  24.996  1.00 73.79      AAAA C
ATOM   4052  CE  LYS   423      26.030  63.374  24.021  1.00 77.06      AAAA C
ATOM   4053  NZ  LYS   423      25.949  64.748  24.614  1.00 64.99      AAAA N
ATOM   4057  C   LYS   423      30.158  65.482  27.071  1.00 57.43      AAAA C
ATOM   4058  O   LYS   423      29.582  65.478  28.152  1.00 55.22      AAAA O
ATOM   4059  N   LEU   424      31.425  65.859  26.862  1.00 55.95      AAAA N
ATOM   4061  CA  LEU   424      32.261  66.162  28.017  1.00 57.07      AAAA C
ATOM   4062  CB  LEU   424      33.463  65.250  28.237  1.00 49.16      AAAA C
ATOM   4063  CG  LEU   424      34.390  65.748  29.370  1.00 68.27      AAAA C
ATOM   4064  CD1 LEU   424      33.821  65.362  30.734  1.00 60.66      AAAA C
ATOM   4065  CD2 LEU   424      35.825  65.276  29.123  1.00 60.35      AAAA C
ATOM   4066  C   LEU   424      32.709  67.585  27.878  1.00 56.29      AAAA C
ATOM   4067  O   LEU   424      33.696  67.861  27.201  1.00 59.98      AAAA O
ATOM   4068  N   CYS   425      31.995  68.488  28.492  1.00 58.76      AAAA N
ATOM   4070  CA  CYS   425      32.342  69.916  28.406  1.00 60.39      AAAA C
ATOM   4071  C   CYS   425      33.771  70.119  28.810  1.00 62.59      AAAA C
ATOM   4072  O   CYS   425      34.288  69.665  29.831  1.00 64.45      AAAA O
ATOM   4073  CB  CYS   425      31.249  70.644  29.214  1.00 68.23      AAAA C
ATOM   4074  SG  CYS   425      29.916  71.303  28.086  1.00 81.03      AAAA S
ATOM   4075  N   VAL   426      34.529  70.953  28.102  1.00 65.31      AAAA N
ATOM   4077  CA  VAL   426      35.943  71.149  28.358  1.00 65.49      AAAA C
ATOM   4078  CB  VAL   426      36.644  72.022  27.310  1.00 66.66      AAAA C
ATOM   4079  CG1 VAL   426      36.715  71.413  25.925  1.00 62.49      AAAA C
ATOM   4080  CG2 VAL   426      35.962  73.365  27.239  1.00 60.92      AAAA C
ATOM   4081  C   VAL   426      36.105  71.711  29.757  1.00 65.99      AAAA C
ATOM   4082  O   VAL   426      37.180  71.724  30.388  1.00 64.51      AAAA O
ATOM   4083  N   SER   427      35.090  72.361  30.267  1.00 67.67      AAAA N
ATOM   4085  CA  SER   427      35.091  72.927  31.599  1.00 66.85      AAAA C
ATOM   4086  CB  SER   427      33.685  73.499  31.864  1.00 61.16      AAAA C
ATOM   4087  OG  SER   427      34.088  74.860  32.098  1.00 67.05      AAAA O
ATOM   4089  C   SER   427      35.515  71.972  32.701  1.00 64.24      AAAA C
ATOM   4090  O   SER   427      36.332  72.328  33.573  1.00 63.66      AAAA O
ATOM   4091  N   GLU   428      34.965  70.771  32.618  1.00 58.75      AAAA N
ATOM   4093  CA  GLU   428      35.384  69.753  33.585  1.00 63.39      AAAA C
ATOM   4094  CB  GLU   428      34.594  68.485  33.240  1.00 68.67      AAAA C
ATOM   4095  CG  GLU   428      33.115  68.560  33.537  1.00 66.59      AAAA C
ATOM   4096  CD  GLU   428      32.785  68.560  35.023  1.00 72.33      AAAA C
ATOM   4097  OE1 GLU   428      32.729  67.522  35.722  1.00 81.62      AAAA O
ATOM   4098  OE2 GLU   428      32.581  69.688  35.517  1.00 70.97      AAAA O
ATOM   4099  C   GLU   428      36.870  69.485  33.429  1.00 61.63      AAAA C
ATOM   4100  O   GLU   428      37.671  69.696  34.307  1.00 62.03      AAAA O
ATOM   4101  N   ILE   429      37.265  69.262  32.165  1.00 61.26      AAAA N
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ATOM   4104  CB  ILE   429      38.759  68.933  30.263  1.00 59.32      AAAA C
ATOM   4105  CG2 ILE   429      40.257  68.915  29.895  1.00 45.93      AAAA C
ATOM   4106  CG1 ILE   429      37.968  67.719  29.794  1.00 57.66      AAAA C
ATOM   4107  CD1 ILE   429      38.038  67.555  28.285  1.00 53.48      AAAA C
ATOM   4108  C   ILE   429      39.498  70.166  32.323  1.00 61.90      AAAA C
ATOM   4109  O   ILE   429      40.592  70.017  32.867  1.00 61.28      AAAA O
ATOM   4110  N   TYR   430      38.987  71.384  32.200  1.00 65.34      AAAA N
ATOM   4112  CA  TYR   430      39.729  72.543  32.719  1.00 68.10      AAAA C
ATOM   4113  CB  TYR   430      39.180  73.822  32.099  1.00 71.02      AAAA C
ATOM   4114  CG  TYR   430      39.538  74.006  30.639  1.00 75.98      AAAA C
ATOM   4115  CD1 TYR   430      38.653  73.821  29.599  1.00 77.60      AAAA C
ATOM   4116  CE1 TYR   430      38.953  73.977  28.270  1.00 75.72      AAAA C
ATOM   4117  CD2 TYR   430      40.810  74.401  30.260  1.00 75.95      AAAA C
ATOM   4118  CE2 TYR   430      41.155  74.575  28.937  1.00 74.81      AAAA C
ATOM   4119  CZ  TYR   430      40.221  74.359  27.952  1.00 78.51      AAAA C
ATOM   4120  OH  TYR   430      40.564  74.542  26.616  1.00 85.40      AAAA O
ATOM   4122  C   TYR   430      39.779  72.634  34.241  1.00 63.72      AAAA C
ATOM   4123  O   TYR   430      40.654  73.321  34.758  1.00 58.26      AAAA O
ATOM   4124  N   ARG   431      38.819  72.017  34.907  1.00 65.53      AAAA N
ATOM   4126  CA  ARG   431      38.747  72.043  36.356  1.00 68.15      AAAA C
ATOM   4127  CB  ARG   431      37.348  71.748  36.898  1.00 73.32      AAAA C
ATOM   4128  CG  ARG   431      37.345  71.815  38.430  1.00 82.99      AAAA C
ATOM   4129  CD  ARG   431      37.270  73.279  38.860  1.00 88.39      AAAA C
ATOM   4130  NE  ARG   431      37.698  73.472  40.258  1.00 92.48      AAAA N
ATOM   4132  CZ  ARG   431      36.835  73.258  41.259  1.00 94.93      AAAA C
ATOM   4133  NH1 ARG   431      35.610  72.872  40.872  1.00 87.40      AAAA N
ATOM   4136  NH2 ARG   431      37.021  73.371  42.567  1.00 95.17      AAAA N
ATOM   4139  C   ARG   431      39.718  70.986  36.877  1.00 67.75      AAAA C
ATOM   4140  O   ARG   431      40.637  71.292  37.629  1.00 66.74      AAAA O
ATOM   4141  N   MET   432      39.541  69.791  36.305  1.00 63.87      AAAA N
ATOM   4143  CA  MET   432      40.437  68.703  36.652  1.00 64.46      AAAA C
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ATOM   4144  CB  MET   432      40.237  67.522  35.719  1.00 54.25      AAAA C
ATOM   4145  CG  MET   432      41.254  66.426  35.971  1.00 40.18      AAAA C
ATOM   4146  SD  MET   432      40.829  64.925  35.112  1.00 52.21      AAAA S
ATOM   4147  CE  MET   432      41.582  63.681  36.137  1.00 54.89      AAAA C
ATOM   4148  C   MET   432      41.891  69.170  36.626  1.00 64.65      AAAA C
ATOM   4149  O   MET   432      42.530  68.992  37.653  1.00 65.88      AAAA O
ATOM   4150  N   GLU   433      42.331  69.811  35.556  1.00 65.78      AAAA N
ATOM   4152  CA  GLU   433      43.622  70.469  35.510  1.00 69.16      AAAA C
ATOM   4153  CB  GLU   433      43.704  71.506  34.401  1.00 69.58      AAAA C
ATOM   4154  CG  GLU   433      44.121  70.967  33.048  1.00 76.91      AAAA C
ATOM   4155  CD  GLU   433      44.623  72.149  32.242  1.00 82.02      AAAA C
ATOM   4156  OE1 GLU   433      44.718  73.224  32.874  1.00 86.82      AAAA O
ATOM   4157  OE2 GLU   433      44.905  72.050  31.042  1.00 88.26      AAAA O
ATOM   4158  C   GLU   433      44.016  71.219  36.781  1.00 71.29      AAAA C
ATOM   4159  O   GLU   433      45.133  71.083  37.294  1.00 74.29      AAAA O
ATOM   4160  N   GLU   434      43.178  72.120  37.280  1.00 72.93      AAAA N
ATOM   4162  CA  GLU   434      43.505  72.873  38.485  1.00 72.86      AAAA C
ATOM   4163  CB  GLU   434      42.458  73.916  38.840  1.00 81.36      AAAA C
ATOM   4164  CG  GLU   434      41.191  73.956  38.032  1.00 83.34      AAAA C
ATOM   4165  CD  GLU   434      40.181  75.004  38.432  1.00 97.32      AAAA C
ATOM   4166  OE1 GLU   434      39.521  74.928  39.505  1.00 97.34      AAAA O
ATOM   4167  OE2 GLU   434      40.080  75.941  37.583  1.00 99.95      AAAA O
ATOM   4168  C   GLU   434      43.675  71.886  39.632  1.00 71.46      AAAA C
ATOM   4169  O   GLU   434      44.728  71.858  40.251  1.00 78.49      AAAA O
ATOM   4170  N   VAL   435      42.670  71.095  39.926  1.00 66.34      AAAA N
ATOM   4172  CA  VAL   435      42.711  70.129  41.001  1.00 62.49      AAAA C
ATOM   4173  CB  VAL   435      41.451  69.217  40.972  1.00 60.38      AAAA C
ATOM   4174  CG1 VAL   435      41.547  68.214  42.104  1.00 52.32      AAAA C
ATOM   4175  CG2 VAL   435      40.203  70.073  41.029  1.00 50.79      AAAA C
ATOM   4176  C   VAL   435      43.939  69.253  41.018  1.00 60.74      AAAA C
ATOM   4177  O   VAL   435      44.607  69.165  42.034  1.00 62.37      AAAA O
ATOM   4178  N   THR   436      44.282  68.506  39.988  1.00 60.67      AAAA N
ATOM   4180  CA  THR   436      45.335  67.516  39.936  1.00 56.36      AAAA C
ATOM   4181  CB  THR   436      45.199  66.565  38.736  1.00 50.92      AAAA C
ATOM   4182  OG1 THR   436      44.913  67.283  37.503  1.00 47.03      AAAA O
ATOM   4184  CG2 THR   436      44.108  65.526  38.901  1.00 54.38      AAAA C
ATOM   4185  C   THR   436      46.701  68.184  39.930  1.00 60.55      AAAA C
ATOM   4186  O   THR   436      47.714  67.490  40.024  1.00 60.61      AAAA O
ATOM   4187  N   GLY   437      46.836  69.496  39.835  1.00 60.65      AAAA N
ATOM   4189  CA  GLY   437      48.102  70.164  39.749  1.00 59.47      AAAA C
ATOM   4190  C   GLY   437      48.800  69.864  38.424  1.00 64.78      AAAA C
ATOM   4191  O   GLY   437      49.983  70.254  38.245  1.00 62.70      AAAA O
ATOM   4192  N   THR   438      48.112  69.387  37.380  1.00 63.79      AAAA N
ATOM   4194  CA  THR   438      48.731  69.169  36.076  1.00 65.09      AAAA C
ATOM   4195  CB  THR   438      47.967  68.027  35.411  1.00 66.87      AAAA C
ATOM   4196  OG1 THR   438      46.600  68.385  35.731  1.00 62.22      AAAA O
ATOM   4198  CG2 THR   438      48.208  66.659  36.019  1.00 68.74      AAAA C
ATOM   4199  C   THR   438      48.590  70.415  35.220  1.00 66.14      AAAA C
ATOM   4200  O   THR   438      49.003  70.543  34.070  1.00 68.05      AAAA O
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ATOM   4203  CA  LYS   439      47.927  72.757  35.154  1.00 71.08      AAAA C
ATOM   4204  CB  LYS   439      47.114  73.708  36.034  1.00 69.23      AAAA C
ATOM   4205  CG  LYS   439      46.677  74.938  35.265  1.00 77.26      AAAA C
ATOM   4206  CD  LYS   439      45.832  75.942  36.014  1.00 81.65      AAAA C
ATOM   4207  CE  LYS   439      44.385  75.475  36.182  1.00 87.39      AAAA C
ATOM   4208  NZ  LYS   439      43.667  76.431  37.100  1.00 93.85      AAAA N
ATOM   4212  C   LYS   439      49.249  73.396  34.752  1.00 73.01      AAAA C
ATOM   4213  O   LYS   439      49.996  73.986  35.541  1.00 74.60      AAAA O
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ATOM   4216  CA  GLY   440      50.733  74.167  33.014  1.00 71.39      AAAA C
ATOM   4217  C   GLY   440      51.716  73.204  32.389  1.00 71.20      AAAA C
ATOM   4218  O   GLY   440      52.684  73.650  31.822  1.00 72.70      AAAA O
ATOM   4219  N   ARG   441      51.445  71.908  32.436  1.00 72.99      AAAA N
ATOM   4221  CA  ARG   441      52.343  70.945  31.831  1.00 74.12      AAAA C
ATOM   4222  CB  ARG   441      52.617  69.740  32.716  1.00 69.44      AAAA C
ATOM   4223  CG  ARG   441      51.847  69.695  34.003  1.00 63.34      AAAA C
ATOM   4224  CD  ARG   441      52.060  68.314  34.595  1.00 67.64      AAAA C
ATOM   4225  NE  ARG   441      52.244  68.395  36.030  1.00 61.00      AAAA N
ATOM   4227  CZ  ARG   441      52.326  67.357  36.831  1.00 59.21      AAAA C
ATOM   4228  NH1 ARG   441      52.258  66.117  36.395  1.00 60.57      AAAA N
ATOM   4231  NH2 ARG   441      52.468  67.596  38.128  1.00 72.94      AAAA N
ATOM   4234  C   ARG   441      51.760  70.446  30.511  1.00 73.50      AAAA C
ATOM   4235  O   ARG   441      52.195  69.424  30.012  1.00 74.73      AAAA O
ATOM   4236  N   GLN   442      50.732  71.114  30.043  1.00 74.69      AAAA N
ATOM   4238  CA  GLN   442      49.959  70.646  28.914  1.00 75.13      AAAA C
ATOM   4239  CB  GLN   442      48.457  70.875  29.126  1.00 68.73      AAAA C
ATOM   4240  CG  GLN   442      47.669  69.576  29.195  1.00 71.20      AAAA C
ATOM   4241  CD  GLN   442      47.623  69.028  30.607  1.00 70.98      AAAA C
ATOM   4242  OE1 GLN   442      47.714  67.822  30.868  1.00 78.66      AAAA O
ATOM   4243  NE2 GLN   442      47.477  69.907  31.584  1.00 66.86      AAAA N
ATOM   4246  C   GLN   442      50.326  71.359  27.627  1.00 77.69      AAAA C
ATOM   4247  O   GLN   442      50.227  72.569  27.530  1.00 75.57      AAAA O
ATOM   4248  N   ALA   443      50.474  70.554  26.575  1.00 81.54      AAAA N
ATOM   4250  CA  ALA   443      50.643  71.148  25.236  1.00 82.95      AAAA C
ATOM   4251  CB  ALA   443      51.104  70.118  24.220  1.00 81.69      AAAA C
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ATOM   4252  C   ALA   443      49.259  71.706  24.952  1.00 83.73      AAAA C
ATOM   4253  O   ALA   443      48.398  71.744  25.830  1.00 83.87      AAAA O
ATOM   4254  N   LYS   444      48.914  72.052  23.713  1.00 86.20      AAAA N
ATOM   4256  CA  LYS   444      47.559  72.524  23.482  1.00 85.88      AAAA C
ATOM   4257  CB  LYS   444      47.426  73.997  23.128  1.00 83.99      AAAA C
ATOM   4258  CG  LYS   444      46.673  74.734  24.241  1.00 93.60      AAAA C
ATOM   4259  CD  LYS   444      45.883  73.841  25.186  1.00 95.14      AAAA C
ATOM   4260  CE  LYS   444      46.390  73.786  26.614  1.00 97.04      AAAA C
ATOM   4261  NZ  LYS   444      45.368  73.090  27.473  1.00 97.22      AAAA N
ATOM   4265  C   LYS   444      46.659  71.779  22.508  1.00 84.20      AAAA C
ATOM   4266  O   LYS   444      45.428  71.901  22.635  1.00 85.63      AAAA O
ATOM   4267  N   GLY   445      47.214  70.734  21.916  1.00 78.85      AAAA N
ATOM   4269  CA  GLY   445      46.368  69.786  21.208  1.00 75.06      AAAA C
ATOM   4270  C   GLY   445      45.803  68.844  22.260  1.00 72.30      AAAA C
ATOM   4271  O   GLY   445      44.963  67.993  21.940  1.00 74.90      AAAA O
ATOM   4272  N   ASP   446      46.300  68.981  23.492  1.00 67.97      AAAA N
ATOM   4274  CA  ASP   446      45.914  68.174  24.642  1.00 62.81      AAAA C
ATOM   4275  CB  ASP   446      46.754  68.552  25.873  1.00 55.24      AAAA C
ATOM   4276  CG  ASP   446      48.213  68.169  25.801  1.00 54.07      AAAA C
ATOM   4277  OD1 ASP   446      48.693  67.385  24.946  1.00 45.08      AAAA O
ATOM   4278  OD2 ASP   446      49.091  68.595  26.593  1.00 50.12      AAAA O
ATOM   4279  C   ASP   446      44.438  68.274  25.016  1.00 58.07      AAAA C
ATOM   4280  O   ASP   446      43.610  67.369  25.127  1.00 55.59      AAAA O
ATOM   4281  N   ILE   447      44.043  69.527  25.226  1.00 54.13      AAAA N
ATOM   4283  CA  ILE   447      42.652  69.822  25.510  1.00 54.09      AAAA C
ATOM   4284  CB  ILE   447      42.505  70.502  26.877  1.00 48.92      AAAA C
ATOM   4285  CG2 ILE   447      41.030  70.663  27.182  1.00 41.02      AAAA C
ATOM   4286  CG1 ILE   447      43.211  69.621  27.932  1.00 52.36      AAAA C
ATOM   4287  CD1 ILE   447      43.468  70.329  29.237  1.00 48.47      AAAA C
ATOM   4288  C   ILE   447      42.027  70.591  24.364  1.00 53.06      AAAA C
ATOM   4289  O   ILE   447      41.718  71.772  24.423  1.00 56.08      AAAA O
ATOM   4290  N   ASN   448      41.625  69.915  23.307  1.00 53.17      AAAA N
ATOM   4292  CA  ASN   448      41.013  70.642  22.202  1.00 54.61      AAAA C
ATOM   4293  CB  ASN   448      41.283  69.982  20.863  1.00 49.17      AAAA C
ATOM   4294  CG  ASN   448      40.415  68.786  20.577  1.00 49.40      AAAA C
ATOM   4295  OD1 ASN   448      39.287  68.977  20.113  1.00 52.34      AAAA O
ATOM   4296  ND2 ASN   448      40.990  67.622  20.871  1.00 52.49      AAAA N
ATOM   4299  C   ASN   448      39.518  70.824  22.402  1.00 56.44      AAAA C
ATOM   4300  O   ASN   448      38.816  69.974  22.939  1.00 55.83      AAAA O
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ATOM   4303  CA  THR   449      37.682  72.351  21.901  1.00 58.62      AAAA C
ATOM   4304  CB  THR   449      37.497  73.845  22.169  1.00 55.90      AAAA C
ATOM   4305  OG1 THR   449      37.913  74.485  20.943  1.00 68.89      AAAA O
ATOM   4307  CG2 THR   449      38.354  74.352  23.310  1.00 59.06      AAAA C
ATOM   4308  C   THR   449      36.920  72.053  20.628  1.00 56.82      AAAA C
ATOM   4309  O   THR   449      35.750  72.381  20.473  1.00 60.87      AAAA O
ATOM   4310  N   ARG   450      37.539  71.304  19.757  1.00 55.76      AAAA N
ATOM   4312  CA  ARG   450      36.887  70.935  18.507  1.00 54.66      AAAA C
ATOM   4313  CB  ARG   450      37.845  71.179  17.377  1.00 48.33      AAAA C
ATOM   4314  CG  ARG   450      38.385  69.975  16.645  1.00 54.81      AAAA C
ATOM   4315  CD  ARG   450      39.487  70.561  15.696  1.00 44.92      AAAA C
ATOM   4316  NE  ARG   450      40.706  70.719  16.488  1.00 52.49      AAAA N
ATOM   4318  CZ  ARG   450      41.544  69.757  16.882  1.00 39.08      AAAA C
ATOM   4319  NH1 ARG   450      41.176  68.572  16.466  1.00 41.07      AAAA N
ATOM   4322  NH2 ARG   450      42.601  70.001  17.610  1.00 45.18      AAAA N
ATOM   4325  C   ARG   450      36.267  69.553  18.557  1.00 56.82      AAAA C
ATOM   4326  O   ARG   450      35.186  69.303  17.992  1.00 58.15      AAAA O
ATOM   4327  N   ASN   451      36.800  68.583  19.324  1.00 56.66      AAAA N
ATOM   4329  CA  ASN   451      36.107  67.311  19.434  1.00 50.27      AAAA C
ATOM   4330  CB  ASN   451      36.725  66.127  18.760  1.00 48.54      AAAA C
ATOM   4331  CG  ASN   451      38.243  66.143  18.764  1.00 60.51      AAAA C
ATOM   4332  OD1 ASN   451      38.779  66.279  19.855  1.00 53.45      AAAA O
ATOM   4333  ND2 ASN   451      38.707  65.976  17.506  1.00 54.88      AAAA N
ATOM   4336  C   ASN   451      35.849  66.854  20.869  1.00 52.97      AAAA C
ATOM   4337  O   ASN   451      35.330  65.750  21.096  1.00 49.71      AAAA O
ATOM   4338  N   ASN   452      36.126  67.668  21.851  1.00 51.98      AAAA N
ATOM   4340  CA  ASN   452      35.769  67.485  23.229  1.00 55.88      AAAA C
ATOM   4341  CB  ASN   452      36.947  67.873  24.136  1.00 54.62      AAAA C
ATOM   4342  CG  ASN   452      37.936  66.736  24.285  1.00 60.96      AAAA C
ATOM   4343  OD1 ASN   452      37.646  65.633  24.735  1.00 51.30      AAAA O
ATOM   4344  ND2 ASN   452      39.153  67.098  23.855  1.00 56.75      AAAA N
ATOM   4347  C   ASN   452      34.603  68.385  23.688  1.00 58.11      AAAA C
ATOM   4348  O   ASN   452      34.785  69.629  23.657  1.00 55.07      AAAA O
ATOM   4349  N   GLY   453      33.444  67.813  23.985  1.00 55.08      AAAA N
ATOM   4351  CA  GLY   453      32.313  68.658  24.296  1.00 59.47      AAAA C
ATOM   4352  C   GLY   453      31.500  69.269  23.174  1.00 64.95      AAAA C
ATOM   4353  O   GLY   453      30.302  69.603  23.276  1.00 65.71      AAAA O
ATOM   4354  N   GLU   454      31.910  69.109  21.910  1.00 67.44      AAAA N
ATOM   4356  CA  GLU   454      31.266  69.543  20.690  1.00 63.63      AAAA C
ATOM   4357  CB  GLU   454      31.739  68.818  19.401  1.00 53.71      AAAA C
ATOM   4358  CG  GLU   454      32.348  67.430  19.738  1.00 49.50      AAAA C
ATOM   4359  CD  GLU   454      32.368  66.620  18.454  1.00 54.61      AAAA C
ATOM   4360  OE1 GLU   454      31.368  66.637  17.702  0.01 54.10      AAAA O
ATOM   4361  OE2 GLU   454      33.417  66.003  18.160  0.01 54.17      AAAA O
ATOM   4362  C   GLU   454      29.762  69.301  20.767  1.00 65.41      AAAA C
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ATOM   4363  O   GLU   454      29.022  70.089  20.169  1.00 67.86      AAAA O
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ATOM   4366  CA  ARG   455      27.843  67.997  21.371  1.00 69.33      AAAA C
ATOM   4367  CB  ARG   455      27.448  66.733  20.652  1.00 73.38      AAAA C
ATOM   4368  CG  ARG   455      28.467  65.912  19.924  1.00 74.27      AAAA C
ATOM   4369  CD  ARG   455      27.775  64.740  19.240  1.00 79.54      AAAA C
ATOM   4370  NE  ARG   455      27.301  63.638  20.052  1.00 86.31      AAAA N
ATOM   4372  CZ  ARG   455      27.802  62.412  20.189  1.00 88.60      AAAA C
ATOM   4373  NH1 ARG   455      28.890  61.997  19.538  1.00 84.51      AAAA N
ATOM   4376  NH2 ARG   455      27.225  61.523  21.003  1.00 87.36      AAAA N
ATOM   4379  C   ARG   455      27.213  67.934  22.756  1.00 67.35      AAAA C
ATOM   4380  O   ARG   455      26.423  67.025  22.961  1.00 66.26      AAAA O
ATOM   4381  N   ALA   456      27.499  68.879  23.623  1.00 66.52      AAAA N
ATOM   4383  CA  ALA   456      26.947  68.906  24.964  1.00 72.01      AAAA C
ATOM   4384  CB  ALA   456      27.832  68.147  25.939  1.00 61.84      AAAA C
ATOM   4385  C   ALA   456      26.802  70.379  25.371  1.00 75.25      AAAA C
ATOM   4386  O   ALA   456      27.706  71.219  25.202  1.00 81.30      AAAA O
ATOM   4387  N   SER   457      25.653  70.720  25.939  0.50 71.91      AAAA N
ATOM   4389  CA  SER   457      25.431  72.095  26.358  0.50 69.64      AAAA C
ATOM   4390  CB  SER   457      23.991  72.247  26.836  0.50 73.30      AAAA C
ATOM   4391  OG  SER   457      23.422  73.294  26.060  0.50 73.31      AAAA O
ATOM   4393  C   SER   457      26.418  72.510  27.437  0.50 69.27      AAAA C
ATOM   4394  O   SER   457      26.458  71.957  28.530  0.50 67.32      AAAA O
ATOM   4395  N   CYS   458      27.197  73.531  27.117  0.50 70.44      AAAA N
ATOM   4397  CA  CYS   458      28.287  73.960  27.972  0.50 72.57      AAAA C
ATOM   4398  C   CYS   458      27.949  75.205  28.757  0.50 72.54      AAAA C
ATOM   4399  O   CYS   458      27.065  75.128  29.606  0.50 76.63      AAAA O
ATOM   4400  CB  CYS   458      29.527  74.171  27.089  0.50 75.38      AAAA C
ATOM   4401  SG  CYS   458      30.844  73.032  27.490  0.50 72.18      AAAA S
ATOM   4402  N   ALA   459      28.607  76.306  28.441  0.50 70.13      AAAA N
ATOM   4404  CA  ALA   459      28.445  77.572  29.116  0.50 70.05      AAAA C
ATOM   4405  CB  ALA   459      27.046  78.149  28.996  0.50 70.57      AAAA C
ATOM   4406  C   ALA   459      28.826  77.461  30.601  0.50 70.13      AAAA C
ATOM   4407  O   ALA   459      29.080  78.556  31.154  0.50 69.96      AAAA O
ATOM   4407  OT  ALA   459      28.855  76.301  31.054  0.50 68.22      AAAA O
ATOM   4522  C1  NAG   461      59.581   7.102  61.119  1.00 88.13      AAAA C
ATOM   4524  C2  NAG   461      59.964   7.338  59.697  1.00 91.94      AAAA C
ATOM   4526  N2  NAG   461      58.738   7.699  58.920  1.00 92.72      AAAA N
ATOM   4528  C7  NAG   461      58.400   9.020  58.999  1.00 96.97      AAAA C
ATOM   4529  O7  NAG   461      58.879   9.774  59.726  1.00 98.62      AAAA O
ATOM   4530  C8  NAG   461      57.323   9.390  58.043  1.00100.60      AAAA C
ATOM   4534  C3  NAG   461      60.725   6.225  59.085  1.00 94.77      AAAA C
ATOM   4536  O3  NAG   461      61.417   6.725  57.930  1.00 98.51      AAAA O
ATOM   4538  C4  NAG   461      61.873   5.869  60.064  1.00 96.01      AAAA C
ATOM   4540  O4  NAG   461      62.661   4.821  59.484  1.00 99.20      AAAA O
ATOM   4542  C5  NAG   461      61.359   5.529  61.474  1.00 95.13      AAAA C
ATOM   4545  C6  NAG   461      62.465   5.321  62.495  1.00 93.66      AAAA C
ATOM   4548  O6  NAG   461      62.745   6.364  63.354  1.00 92.13      AAAA O
ATOM   4544  O5  NAG   461      60.625   6.648  61.949  1.00 91.92      AAAA O
ATOM   4550  C1  NAG   463      33.054  15.249  72.938  1.00 43.58      AAAA C
ATOM   4552  C2  NAG   463      31.644  15.282  73.412  1.00 43.62      AAAA C
ATOM   4554  N2  NAG   463      30.709  14.527  72.541  1.00 42.16      AAAA N
ATOM   4556  C7  NAG   463      29.912  13.584  73.099  1.00 40.84      AAAA C
ATOM   4557  O7  NAG   463      29.928  13.406  74.222  1.00 40.10      AAAA O
ATOM   4558  C8  NAG   463      28.975  12.694  72.394  1.00 35.47      AAAA C
ATOM   4562  C3  NAG   463      31.150  16.675  73.448  1.00 45.40      AAAA C
ATOM   4564  O3  NAG   463      29.979  16.555  74.196  1.00 45.99      AAAA O
ATOM   4566  C4  NAG   463      32.117  17.617  74.171  1.00 50.36      AAAA C
ATOM   4568  O4  NAG   463      31.596  18.919  73.891  1.00 53.97      AAAA O
ATOM   4569  C5  NAG   463      33.589  17.477  73.725  1.00 48.50      AAAA C
ATOM   4572  C6  NAG   463      34.490  17.996  74.742  1.00 48.34      AAAA C
ATOM   4575  O6  NAG   463      34.906  18.739  75.671  1.00 57.11      AAAA O
ATOM   4571  O5  NAG   463      33.942  16.120  73.583  1.00 48.58      AAAA O
ATOM   4576  C1  FUC   464      34.544  19.954  76.083  1.00 81.45      AAAA C
ATOM   4578  C2  FUC   464      35.179  21.173  75.463  1.00 86.35      AAAA C
ATOM   4579  O2  FUC   464      35.153  21.169  74.021  1.00 92.94      AAAA O
ATOM   4582  C3  FUC   464      34.252  22.284  75.945  1.00 86.79      AAAA C
ATOM   4584  O3  FUC   464      34.691  23.613  75.596  1.00 87.83      AAAA O
ATOM   4586  C4  FUC   464      33.871  22.274  77.412  1.00 86.67      AAAA C
ATOM   4588  O4  FUC   464      34.598  23.297  78.115  1.00 87.06      AAAA O
ATOM   4590  C5  FUC   464      33.921  20.894  78.040  1.00 85.85      AAAA C
ATOM   4593  C6  FUC   464      34.279  20.768  79.512  1.00 83.37      AAAA C
ATOM   4592  O5  FUC   464      35.042  20.150  77.425  1.00 82.43      AAAA O
ATOM   4597  C1  NAG   465      31.575  19.813  74.940  1.00 64.68      AAAA C
ATOM   4599  C2  NAG   465      31.267  21.207  74.437  1.00 69.57      AAAA C
ATOM   4601  N2  NAG   465      32.480  21.642  73.690  1.00 71.25      AAAA N
ATOM   4603  C7  NAG   465      32.401  21.953  72.381  1.00 73.86      AAAA C
ATOM   4604  O7  NAG   465      31.373  21.835  71.881  1.00 74.80      AAAA O
ATOM   4605  C8  NAG   465      33.679  22.401  71.787  1.00 76.00      AAAA C
ATOM   4609  C3  NAG   465      31.050  22.214  75.546  1.00 72.71      AAAA C
ATOM   4611  O3  NAG   465      30.713  23.517  75.108  1.00 71.03      AAAA O
ATOM   4613  C4  NAG   465      30.035  21.654  76.560  1.00 75.71      AAAA C
ATOM   4615  O4  NAG   465      29.993  22.409  77.793  1.00 76.79      AAAA O
ATOM   4617  C5  NAG   465      30.498  20.238  76.977  1.00 75.45      AAAA C
ATOM   4620  C6  NAG   465      29.461  19.647  77.930  1.00 75.64      AAAA C
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ATOM   4623  O6  NAG   465      28.385  19.238  77.142  1.00 76.25      AAAA O
ATOM   4619  O5  NAG   465      30.514  19.425  75.807  1.00 71.44      AAAA O
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ATOM   4632  O7  NAG   467      49.541  12.267  91.586  1.00105.48      AAAA O
ATOM   4633  C8  NAG   467      48.526  14.239  91.102  1.00105.02      AAAA C
ATOM   4637  C3  NAG   467      51.967  12.134  88.802  1.00101.03      AAAA C
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ATOM   4645  C5  NAG   467      52.039  10.160  87.218  1.00100.16      AAAA C
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ATOM   4687  O3  FUC   470      53.381  49.515  72.637  1.00 56.30      AAAA O
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ATOM   4716  C4  NAG   471      59.645  48.488  72.694  1.00 38.52      AAAA C
ATOM   4718  O4  NAG   471      59.754  49.464  73.694  1.00 37.44      AAAA O
ATOM   4719  C5  NAG   471      59.056  48.958  71.332  1.00 36.94      AAAA C
ATOM   4722  C6  NAG   471      60.116  49.692  70.525  1.00 36.14      AAAA C
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ATOM   4727  C1  MAN   472      61.035  49.984  73.959  1.00 53.37      AAAA C
ATOM   4729  C2  MAN   472      60.920  51.497  74.260  1.00 56.72      AAAA C
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ATOM   4733  C3  MAN   472      62.216  52.031  74.840  1.00 60.70      AAAA C
ATOM   4735  O3  MAN   472      62.028  53.337  75.383  1.00 60.70      AAAA O
ATOM   4736  C4  MAN   472      62.787  51.161  75.932  1.00 55.46      AAAA C
ATOM   4738  O4  MAN   472      64.085  51.595  76.171  1.00 57.16      AAAA O
ATOM   4740  C5  MAN   472      62.797  49.685  75.511  1.00 52.19      AAAA C
ATOM   4743  C6  MAN   472      63.458  48.905  76.595  1.00 50.32      AAAA C
ATOM   4746  O6  MAN   472      62.990  48.969  77.885  1.00 51.02      AAAA O
ATOM   4742  O5  MAN   472      61.443  49.407  75.200  1.00 53.33      AAAA O
ATOM   4748  C1  MAN   473      62.594  54.401  74.672  1.00 72.61      AAAA C
ATOM   4750  C2  MAN   473      62.417  55.679  75.569  1.00 75.28      AAAA C
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ATOM   4760  O4  MAN   473      58.983  56.571  74.178  1.00 78.93      AAAA O
ATOM   4762  C5  MAN   473      60.499  54.802  73.474  1.00 76.89      AAAA C
ATOM   4765  C6  MAN   473      59.968  54.490  72.091  1.00 74.73      AAAA C
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ATOM   4420  C   ALA   480      36.306  75.030  16.849  1.00 91.39      BBBB C
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ATOM   4421  O   ALA   480      35.415  74.647  17.610  1.00 93.79      BBBB O
ATOM   4422  N   GLN   481      36.135  75.304  15.564  0.01 89.69      BBBB N
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ATOM   4425  CB  GLN   481      34.471  76.492  14.224  0.01 92.74      BBBB C
ATOM   4426  CG  GLN   481      34.277  77.627  15.220  1.00 99.93      BBBB C
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ATOM   4469  OG  SER   485      43.190  70.035  13.376  1.00 63.03      BBBB O
ATOM   4471  C   SER   485      43.294  67.711  12.240  1.00 50.57      BBBB C
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ATOM   4770  S   SUL   493      37.234  -7.808  65.465  1.00108.87      DDDD S
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ATOM   4776  O1  SUL   494      56.597  19.128  67.659  1.00107.98      DDDD O
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ATOM   4783  O3  SUL   495      33.552  11.860  74.748  1.00112.77      DDDD O
ATOM   4784  O4  SUL   495      33.773  10.278  76.604  1.00113.18      DDDD O
ATOM   4785  S   SUL   496      35.466  24.844  59.093  1.00 50.73      DDDD S
ATOM   4786  O1  SUL   496      35.613  24.843  60.607  1.00 62.59      DDDD O
ATOM   4787  O2  SUL   496      36.002  23.581  58.571  1.00 48.59      DDDD O
ATOM   4788  O3  SUL   496      35.880  26.084  58.455  1.00 56.74      DDDD O
ATOM   4789  O4  SUL   496      33.958  24.953  59.034  1.00 59.34      DDDD O
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ATOM   4791  O1  SUL   497      47.849  -1.058  70.996  1.00 68.52      DDDD O
ATOM   4792  O2  SUL   497      48.594  -2.509  69.072  1.00 70.94      DDDD O
ATOM   4793  O3  SUL   497      46.187  -2.393  69.810  1.00 73.47      DDDD O
ATOM   4794  O4  SUL   497      47.799  -3.446  71.129  1.00 71.33      DDDD O
ATOM   4795  S   SUL   498      56.527  35.758  75.513  1.00 71.48      DDDD S
ATOM   4796  O1  SUL   498      55.870  35.013  76.621  1.00 72.97      DDDD O
ATOM   4797  O2  SUL   498      57.759  34.996  75.167  1.00 69.11      DDDD O
ATOM   4798  O3  SUL   498      56.619  37.237  75.785  1.00 72.45      DDDD O
ATOM   4799  O4  SUL   498      55.623  35.809  74.330  1.00 72.74      DDDD O
ATOM   4800  S   SUL   499      40.639  27.365  69.499  1.00 74.04      DDDD S
ATOM   4801  O1  SUL   499      40.218  26.039  70.045  1.00 76.00      DDDD O
ATOM   4802  O2  SUL   499      42.089  27.608  69.835  1.00 75.15      DDDD O
ATOM   4803  O3  SUL   499      39.823  28.467  70.098  1.00 77.27      DDDD O
ATOM   4804  O4  SUL   499      40.424  27.245  68.018  1.00 75.70      DDDD O
ATOM   4805  S   SUL   500      44.996  53.228  20.568  1.00 83.89      DDDD S
ATOM   4806  O1  SUL   500      45.080  54.400  21.461  1.00 84.79      DDDD O
ATOM   4807  O2  SUL   500      46.109  52.266  20.827  1.00 90.38      DDDD O
ATOM   4808  O3  SUL   500      45.032  53.674  19.135  1.00 92.23      DDDD O
ATOM   4809  O4  SUL   500      43.762  52.396  20.723  1.00 91.61      DDDD O
ATOM   4810  OW  WAT   501      29.970   6.904  77.713  1.00 34.84      DDDD O
ATOM   4813  OW  WAT   502      42.522  18.998  78.232  1.00 55.27      DDDD O
ATOM   4816  OW  WAT   503      37.561  21.003  67.518  1.00 41.63      DDDD O
ATOM   4819  OW  WAT   504      50.446   5.721  63.485  1.00 57.37      DDDD O
ATOM   4822  OW  WAT   505      56.668  24.854  72.729  1.00 57.34      DDDD O
ATOM   4825  OW  WAT   506      50.605  57.695  22.727  1.00 54.26      DDDD O
ATOM   4828  OW  WAT   507      55.123  37.781  61.204  1.00 43.71      DDDD O
ATOM   4831  OW  WAT   508      17.414  -9.070  74.793  1.00 48.79      DDDD O
ATOM   4834  OW  WAT   509      44.263  20.885  63.811  1.00 28.64      DDDD O
ATOM   4837  OW  WAT   510      45.085  19.708  84.433  1.00 49.09      DDDD O
ATOM   4840  OW  WAT   511      33.537   1.927  71.115  1.00 60.39      DDDD O
ATOM   4843  OW  WAT   512      19.279   4.902  75.254  1.00 55.23      DDDD O
ATOM   4846  OW  WAT   513      11.502  -0.835  68.996  1.00 57.51      DDDD O
ATOM   4849  OW  WAT   514      24.591  17.207  56.665  1.00 56.36      DDDD O
ATOM   4852  OW  WAT   515      56.947  34.914  62.552  1.00 36.47      DDDD O
ATOM   4855  OW  WAT   516      58.092  39.983  66.234  1.00 30.34      DDDD O
ATOM   4858  OW  WAT   517      48.308  40.726  56.768  1.00 81.69      DDDD O
ATOM   4861  OW  WAT   518      25.776   2.355  85.630  1.00 66.34      DDDD O
ATOM   4864  OW  WAT   519      30.644  68.108  30.765  1.00 82.28      DDDD O
ATOM   4867  OW  WAT   520      38.739  54.257  43.611  1.00 43.41      DDDD O
ATOM   4870  OW  WAT   521      22.886   4.470  64.871  1.00 48.71      DDDD O
ATOM   4873  OW  WAT   522      30.938  50.249  19.364  1.00 54.00      DDDD O
ATOM   4876  OW  WAT   523      32.413   9.061  42.441  1.00 44.45      DDDD O
ATOM   4879  OW  WAT   524      41.019  42.560  55.653  1.00 43.40      DDDD O
ATOM   4882  OW  WAT   525      54.268  51.393  37.513  1.00 55.10      DDDD O
ATOM   4885  OW  WAT   526      37.130  13.599  81.397  1.00 46.49      DDDD O
ATOM   4888  OW  WAT   527      42.585  10.244  84.472  1.00 35.95      DDDD O
ATOM   4891  OW  WAT   528      43.661  61.633  18.450  1.00 41.05      DDDD O
ATOM   4894  OW  WAT   529      27.980  19.862  53.348  1.00 54.59      DDDD O
ATOM   4897  OW  WAT   530      59.527  38.520  64.116  1.00 37.96      DDDD O
ATOM   4900  OW  WAT   531      22.451   1.046  57.437  1.00 59.31      DDDD O
ATOM   4903  OW  WAT   532      30.380  16.123  70.205  1.00 40.39      DDDD O
ATOM   4906  OW  WAT   533      46.835  27.888  65.854  1.00 52.34      DDDD O
ATOM   4909  OW  WAT   534      39.446  49.001  45.379  1.00 46.05      DDDD O
ATOM   4912  OW  WAT   535      46.992  51.272  50.722  1.00 52.62      DDDD O
ATOM   4915  OW  WAT   536      44.263  18.776  73.017  1.00 40.61      DDDD O
ATOM   4918  OW  WAT   537      33.670  58.861  20.848  1.00 51.56      DDDD O
ATOM   4921  OW  WAT   538      52.469  21.639  73.804  1.00 61.98      DDDD O
ATOM   4924  OW  WAT   539      49.985  44.871  37.324  1.00 45.45      DDDD O
ATOM   4927  OW  WAT   540      24.074  -1.791  60.077  1.00 40.40      DDDD O
ATOM   4930  OW  WAT   541      35.207   0.714  79.039  1.00 51.34      DDDD O
ATOM   4933  OW  WAT   542      31.231  -1.176  62.362  1.00 48.33      DDDD O
ATOM   4936  OW  WAT   543      41.726  -5.156  55.290  1.00 60.67      DDDD O
ATOM   4939  OW  WAT   544      48.564  37.335  72.612  1.00 71.69      DDDD O
ATOM   4942  OW  WAT   545      49.501  40.030  67.582  1.00 44.88      DDDD O
ATOM   4945  OW  WAT   546      54.851   7.987  60.018  1.00 49.91      DDDD O
```

```
ATOM   4948  OW  WAT   547      30.459 -14.058  70.554  1.00 84.42      DDDD O
ATOM   4951  OW  WAT   548      57.310  32.779  60.848  1.00 50.77      DDDD O
END
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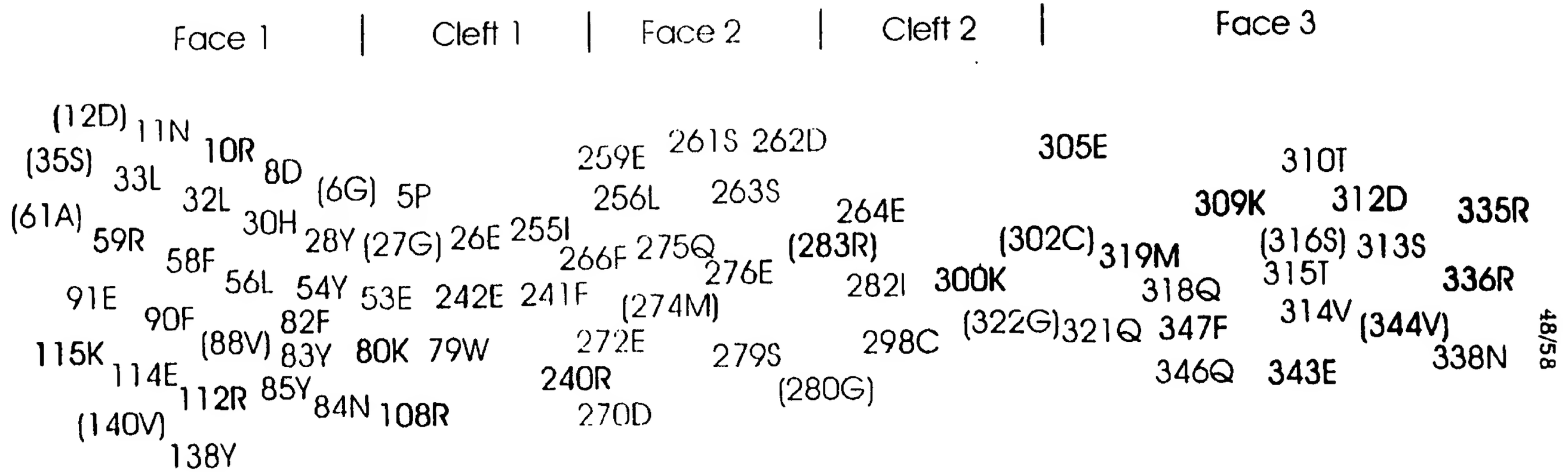
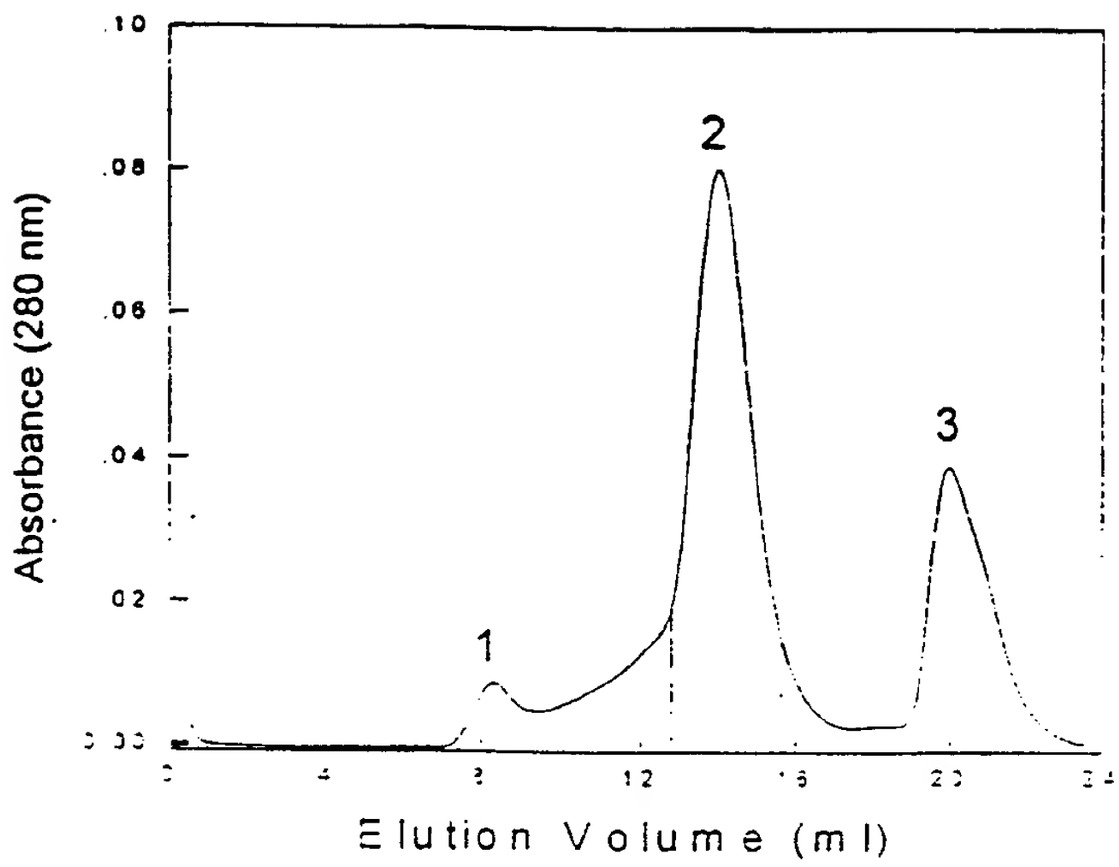

Face 1
Cleft 1
Face 2
Cleft 2
Face 3
(12D)
11N
10R
8D
(35S)
33L
32L
30H
(6G)
5P
259E
261S
262D
305E
310T
(61A)
59R
28Y
(27G)
26E
255I
256L
263S
264E
309K
312D
335R
58F
266F
275Q
(283R)
(302C)
319M
(316S)
313S
91E
56L
54Y
53E
242E
241F
276E
282I
300K
315T
336R
90F
82F
(274M)
318Q
314V
115K
(88V)
83Y
80K
79W
272E
298C
(322G)
321Q
347F
(344V)
48/58
114E
85Y
240R
279S
346Q
343E
338N
112R
84N
108R
(280G)
(140V)
270D
138Y

Figure 2

(a)


Absorbance (280 nm)
.10
.08
.06
.04
.02
1
2
3
Elution Volume (ml)

(b)

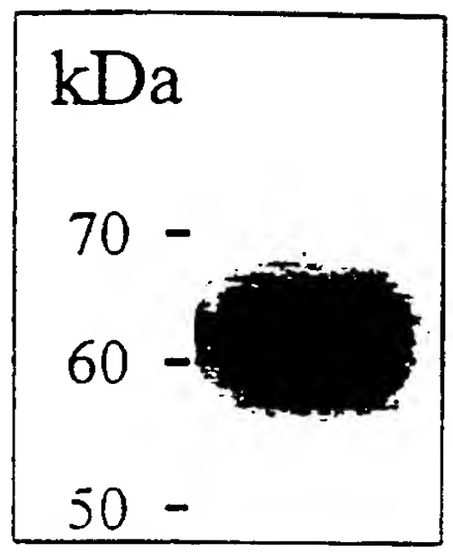
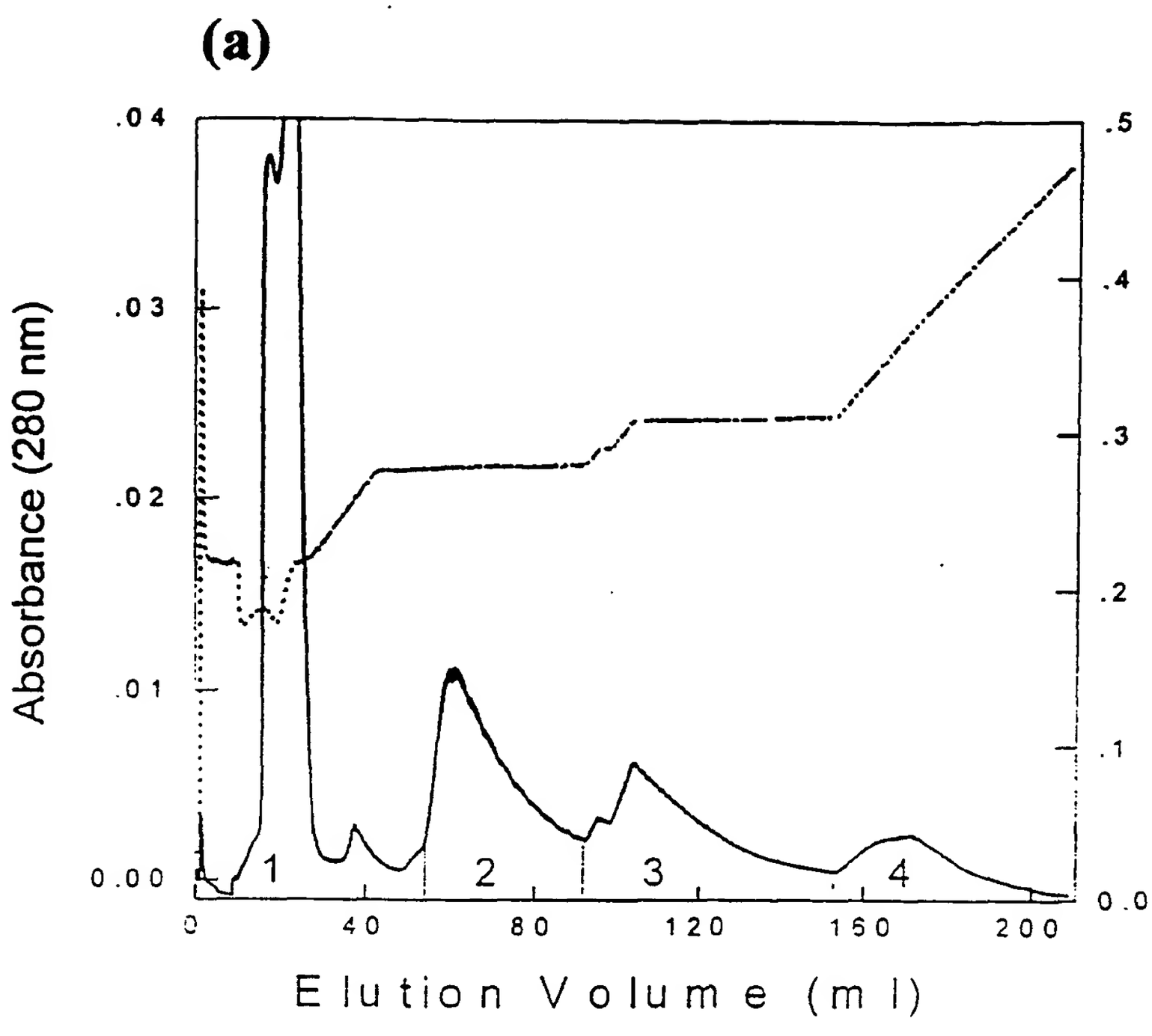
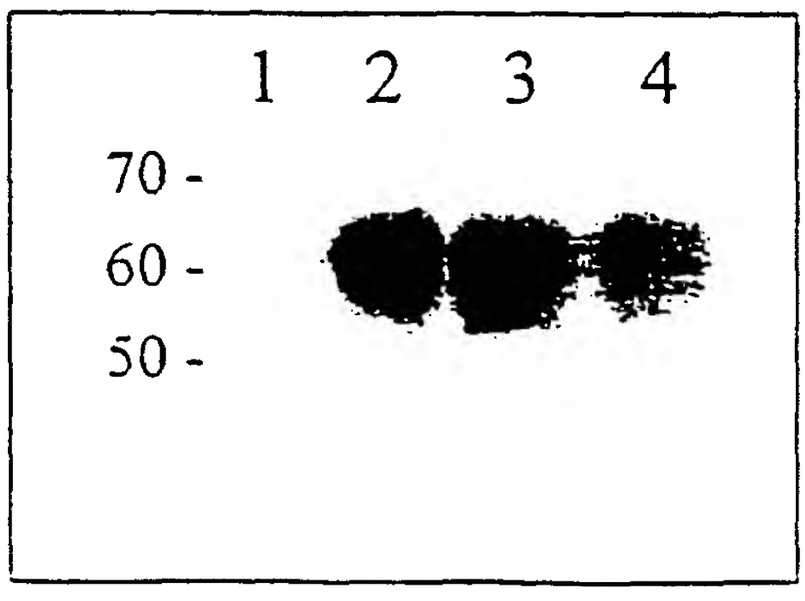

kDa
70
60
50

Figure 3


(a)
.04
.03
.02
.01
0.00
Absorbance (280 nm)
.5
.4
.3
.2
.1
0.0
Conductivity mS/cm
1
2
3
4
0
40
80
120
160
200
Elution Volume (ml)

(b)


1 2 3 4
70 -
60 -
50 -

(c)


2

Figure 4

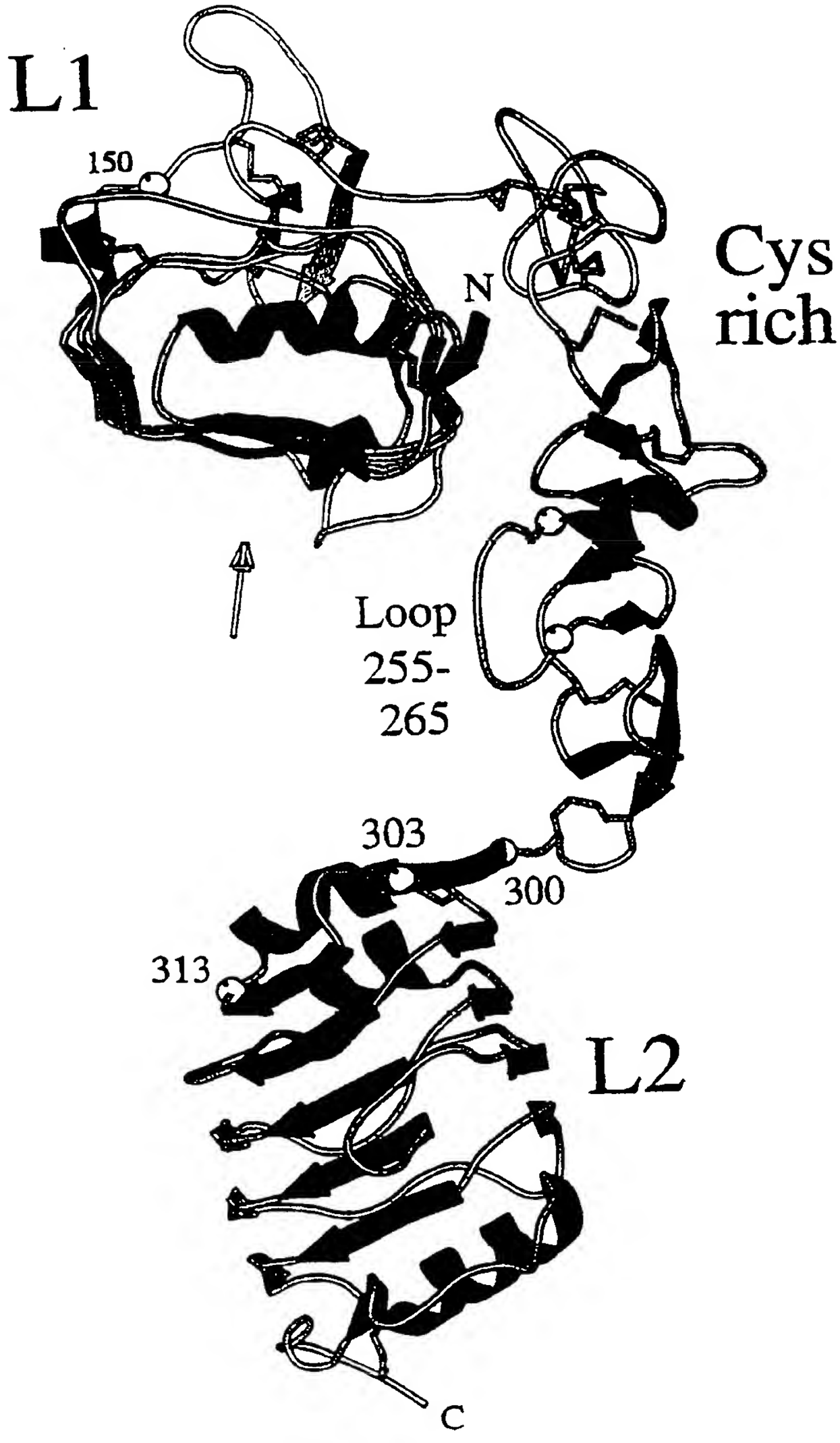


Figure 5

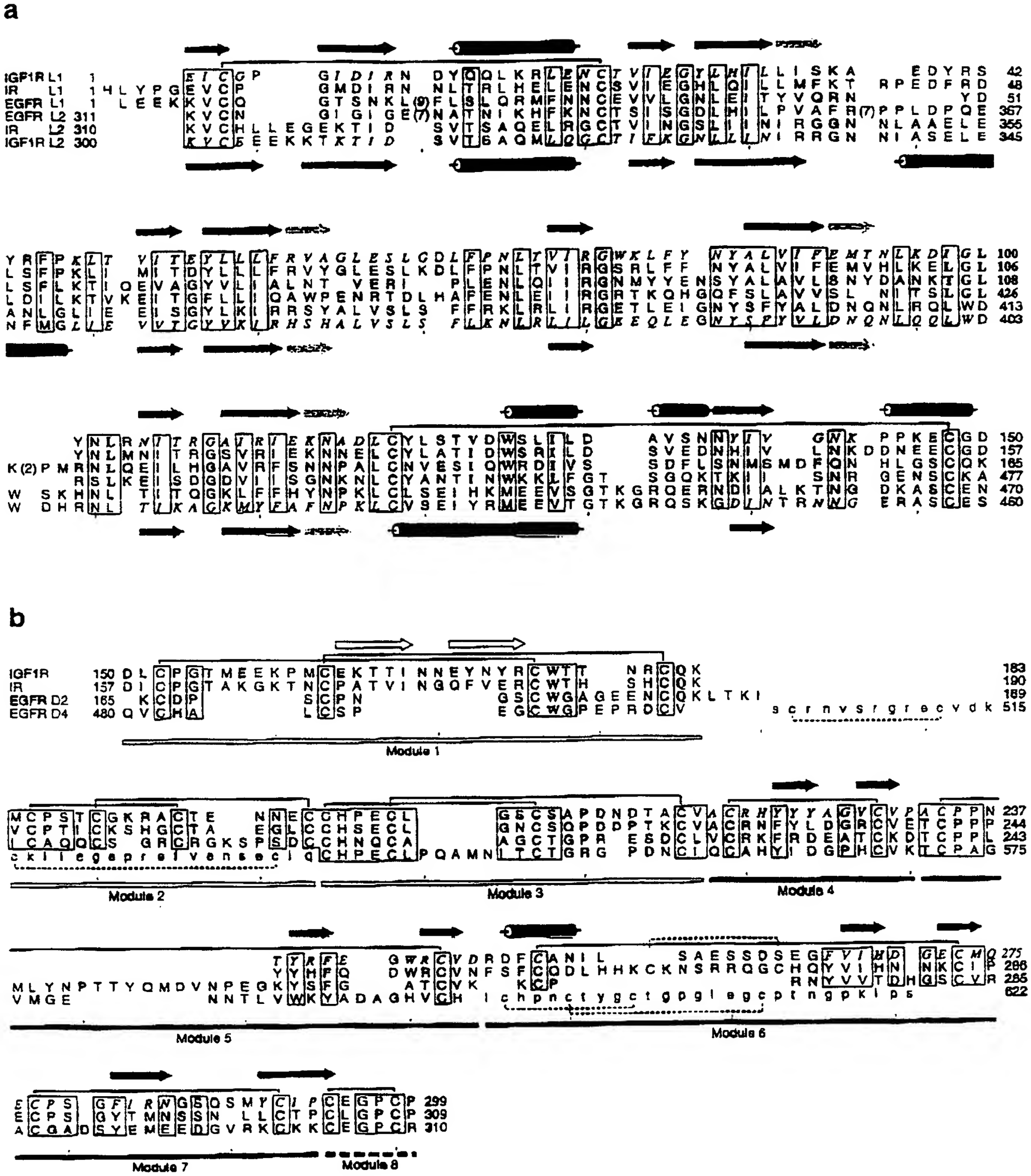

a
b
Module 1
Module 2
Module 3
Module 4
Module 5
Module 6
Module 7
Module 8

Figure 6

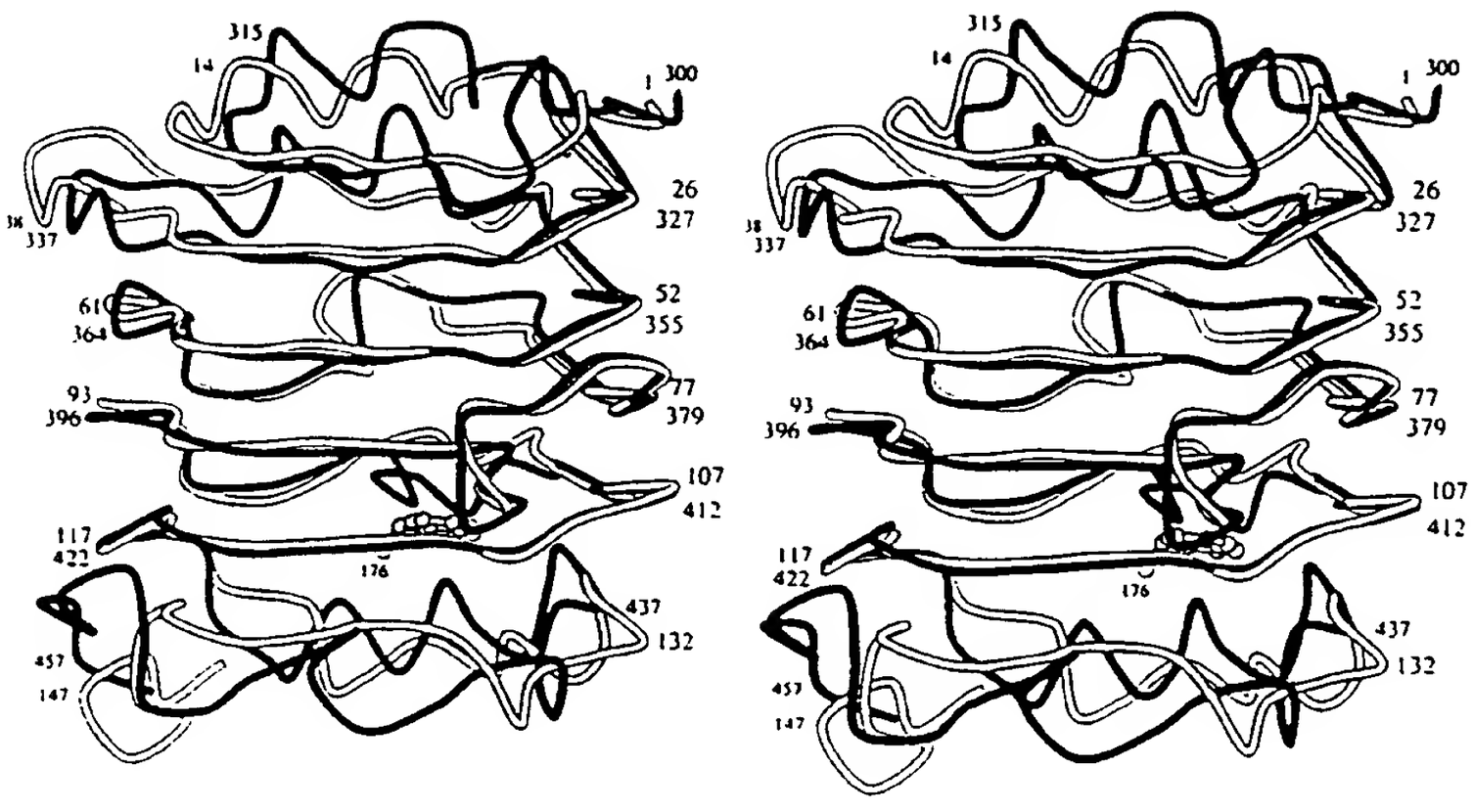

315
14
1
300
26
327
38
337
52
355
61
364
77
379
93
396
107
412
117
422
176
437
132
457
147

Figure 7

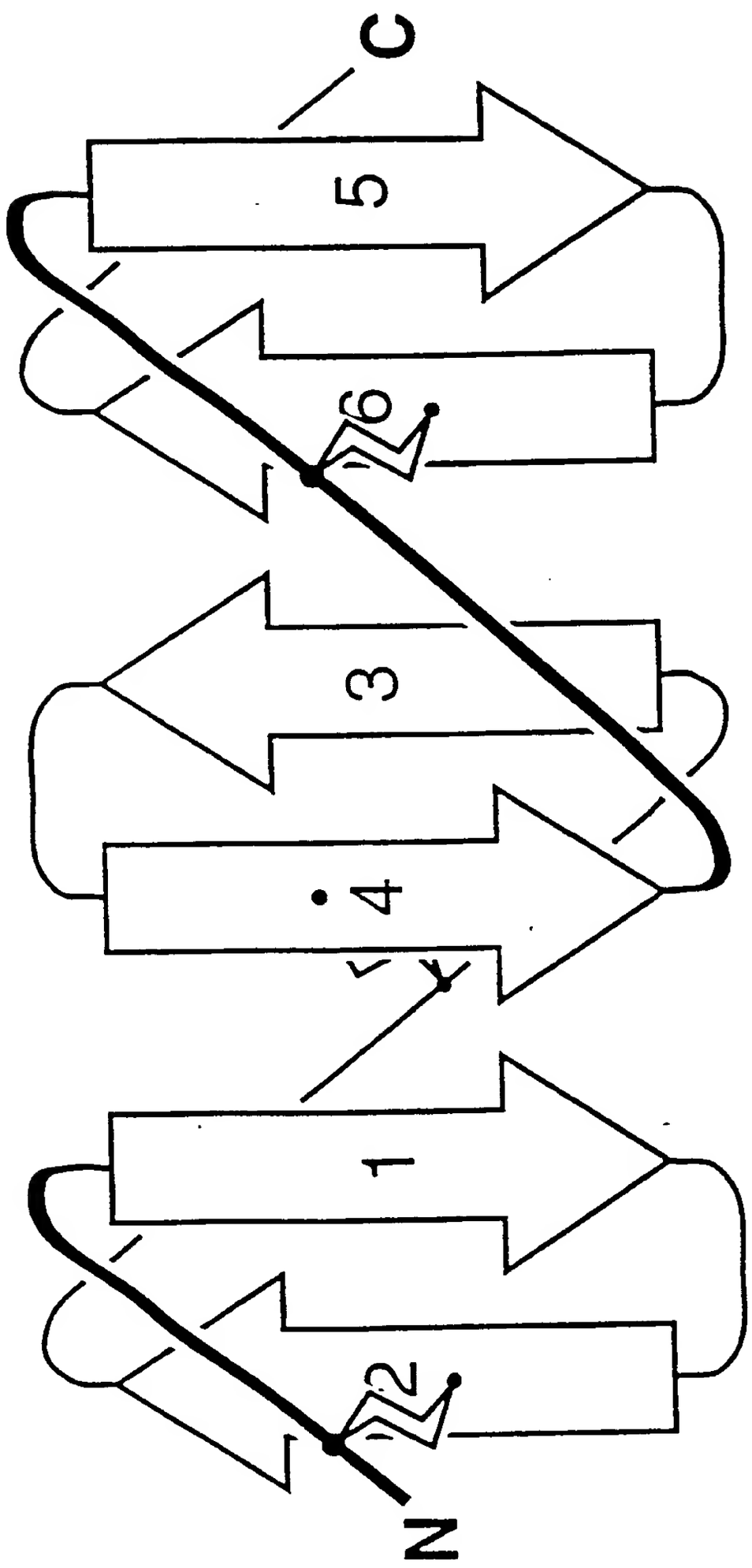


Figure 8

Figure 9: Sequence Alignment of hIGF-1R, hIR and hIRR ectodomains.

Derived by use of the PileUp program in the software package of the Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA.

```
Symbol Comparison table: GenRunData:PileUpPep.Cmp  CompCheCk: 1254

                    GapWeight: 3.0
              GapLengthWeight: 0.1


Name: Higflr          Len:   972  CheCk: 1781  Weight:  1.00
Name: Hir             Len:   972  CheCk: 2986  Weight:  1.00
Name: Hirr            Len:   972  CheCk: 9819  Weight:  1.00

                                  *                   *
Higflr  .....EICGP GIDIRNDYQQ LKRLENCTVI EGYLHILLIS K..AEDYRSY 43
  Hir   HLYPGEVC.P GMDIRNNLTR LHELENCSVI EGHLQILLMF KTRPEDFRDL 49
  Hirr  ....MNVC.P SLDIRSEVAE LRQLENCSVV EGHLQILLMF TATGEDFRGL 45

Higflr  RFPKLTVITE YLLLFRVAGL ESLGDLFPNL TVIRGWKLFY NYALVIFEMT 93
  Hir   SFPKLIMITD YLLLFRVYGL ESLKDLFPNL TVIRGSRLFF NYALVIFEMV 99
  Hirr  SFPRLTQVTD YLLLFRVYGL ESLRDLFPNL AVIRGTRLFL GYALVIFEMP 95

                                        *
Higflr  NLKDIGLYNL RNITRGAIRI EKNADLCYLS TVDWSLILDA VSNNYIVGNK 143
  Hir   HLKELGLYNL MNITRGSVRI EKNNELCYLA TIDWSRILDS VEDNYIVLNK 149
  Hirr  HLRDVALPAL GAVLRGAVRV EKNQELCHLS TIDWGLLQPA PGANHIVGNK 145

                *   *             *               *     *   *
Higflr  PPK.ECGDLC PGTMEEKPM. CEKTTINNEY NYRCWTTNRC QKMCPSTCGK 191
  Hir   DDNEECGDIC PGTAKGKTN. CPATVINGQF VERCWTHSHC QKVCPTICKS 198
  Hirr  LG.EECADVC PGVLGAAGEP CAKTTFSGHT DYRCWTSSHC QRVCPCPHG. 193

                *     **    *   *           *  *           *    *
Higflr  RACTENNECC HPECLGSCSA PDNDTACVAC RHYYYAGVCV PACPPNTYRF 241
  Hir   HGCTAEGLCC HSECLGNCSQ PDDPTKCVAC RNFYLDGRCV ETCPPPYYHF 248
  Hirr  MACTARGECC HTECLGGCSQ PEDPRACVAC RHLYFQGACL WACPPGTYQY 243

                    *       *       *---------*           *   *
Higflr  EGWRCVDRDF CANILSAES. ...SDSEGFV IHDGECMQEC PSGFIRNGSQ 287
  Hir   QDWRCVNFSF CQDLHHKCKN SRRQGCHQYV IHNNKCIPEC PSGYTMNSSN 298
  Hirr  ESWRCVTAER CASLHSVPG. ....RASTFG IHQGSCLAQC PSGFTRNSS. 287

                      *   *     *   *                     *
Higflr  SMYCIPCEGP CPKVCEEEKK TKTIDSVTSA QMLQGCTIFK GNLLINIRRG 337
  Hir   .LLCTPCLGP CPKVCHLLEG EKTIDSVTSA QELRGCTVIN GSLIINIRGG 347
  Hirr  SIFCHKCEGL CPKECKV..G TKTIDSIQAA QDLVGCTHVE GSLILNLRQG 335

Higflr  NNIASELENF MGLIEVVTGY VKIRHSHALV SLSFLKNLRL ILGEEQLEGN  387
  Hir   NNLAAELEAN LGLIEEISGY LKIRRSYALV SLSFFRKLRL IRGETLEIGN  397
  Hirr  YNLEPQLQHS LGLVETITGF LKIKHSFALV SLGFFKNLKL IRGDAMVDGN  385

                                                      *
Higflr  YSFYVLDNQN LQQLWDWDHR NLTIKAGKMY FAFNPKLCVS EIYRMEEVTG  437
  Hir   YSFYALDNQN LRQLWDWSKH NLTITQGKLF FHYNPKLCLS EIHKMEEVSG  447
  Hirr  YTLYVLDNQN LQQLGSWVAA GLTIPVGKIY FAFNPRLCLE HIYRLEEVTG  435
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                                        *     !End of 1-462 fragment
Higflr  TKGRQSKGDI NTRNNGERAS CESDV  LHFTS TTTSKNRIII TWHRYRPPDY  487
   Hir  TKGRQERNDI ALKTNGDQAS CENEL  LKFSY IRTSFDKILL RWEPYWPPDF  497
  Hirr  TRGRQNKAEI NPRTNGDRAA CQTRT  LRFVS NVTEADRILL RWERYEPLEA  485
*
Higflr  RDLISFTVYY KEAPFKNVTE YDGQDACGSN SWNMVDVDLP .....PNKDV  532
   Hir  RDLLGFMLFY KEAPYQNVTE FDGQDACGSN SWTVVDIDPP LRSNDPKSQN  547
  Hirr  RDLLSFIVYY KESPFQNATE HVGPDACGTQ SWNLLDVELP L.....SRTQ  530


Higflr  EPGILLHGLK PWTQYAVYVK AVTLTMVEND HIRGAKSEIL YIRTNASVPS  582
   Hir  HPGWLMRGLK PWTQYAIFVK TL.VTFSDER RTYGAKSDII YVQTDATNPS  596
  Hirr  EPGVTLASLK PWTQYAVFVR AITLTTEEDS PHQGAQSPIV YLRTLPAAPT  580


Higflr  IPLDVLSASN SSSQLIVKWN PPSLPNGNLS YYIVRWQRQP QDGYLYRHNY  632
   Hir  VPLDPISVSN SSSQIILKWK PPSDPNGNIT HYLVFWERQA EDSELFELDY  646
  Hirr  VPQDVISTSN SSSHLLVRWK PPTQRNGNLT YYLVLWQRLA EDGDLYLNDY  630

        *                                 *   ** **  *
Higflr  CSKD.KIPIR KYADGTIDIE EVTENPKTEV CGGEKGPCCA C...PKTEAE  678
   Hir  CLKGLKLPSR TWS.PPFESE DSQKHNQSE. YEDSAGECCS C...PKTDSQ  691
  Hirr  CHRGLRLPTS N.NDPRFDGE DGDPEAEME. .....SDCCP CQHPPPGQVL  673

                                      α------><------β
Higflr  KQAEKEEAEY RKVFENFLHN SIFVPRPERK RRDVMQVANT TMSSRSRNTT  728
   Hir  ILKELEESSF RKTFEDYLHN VVFVPRPSRK RRSLGDVGNV TVAVP...TV  738
  Hirr  PPLEAQEASF QKKFENFLHN AITIPISPWK VTSINKSPQR D.SGRHRRAA  722

                                                             *
Higflr  AA..DTYNIT DPEELETEYP FFESRVDNKE RTVISNLRPF TLYRIDIHSC 776
   Hir  AAFPNTSSTS VPTSPEEHRP F..EKVVNKE SLVISGLRHF TGYRIELQAC 786
  Hirr  GPLRLGGNSS DFEIQEDKVP ........RE RAVLSGLRHF TEYRIDIHAC 764

              *
Higflr  NHEAEKLGCS ASNFVFARTM PAEGADDIPG PVTWEPRPEN SIFLKWPEPE 826
   Hir  NQDTPEERCS VAAYVSARTM PEAKADDIVG PVTHEIFENN VVHLMWQEPK 836
  Hirr  NHAAHTVGCS AATFVFARTM PHREADGIPG KVAWEASSKN SVLLRWLEPP 814

                                    *               *
Higflr  NPNGLILMYE IKYGS.QVED QRECVSRQEY RKYGGAKLNR LNPGNYTARI 875
   Hir  EPNGLIVLYE VSYRRYGDEE LHLCVSRKHF ALERGCRLRG LSPGNYSVRI 886
  Hirr  DPNGLILKYE IKYRRLGEEA TVLCVSRLRY AKFGGVHLAL LPPGNYSARV 864

Higflr  QATSLSGNGS WTDPVFFYVQ AKTGYENFIH L                     906
   Hir  RATSLAGNGS WTEPTYFYVT DYLDVPSNIA K                     917
  Hirr  RATSLAGNGS WTDSVAFYIL GPEEEDAGGL H                     895
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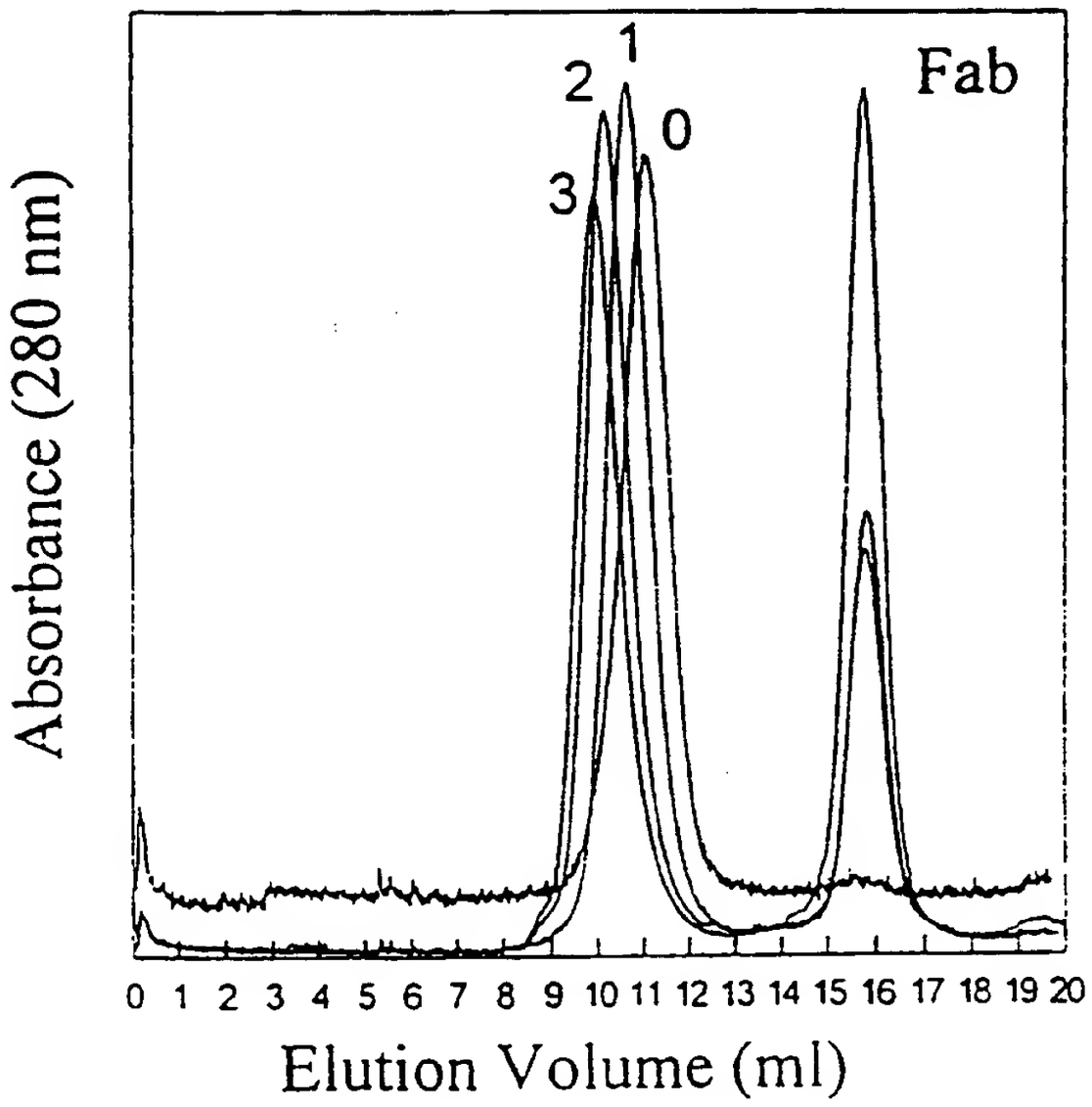

1
2
0
3
Fab
Absorbance (280 nm)
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Elution Volume (ml)

Figure 10

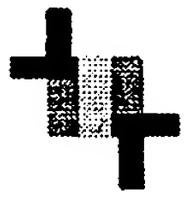
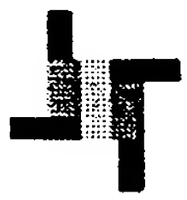
Schematic interpretations of EM images			
Sample	Projection along: y axis	z axis	x axis
hIR			
hIR/ 83-7			
hIR/ 83-14			
hIR/ 18-44/83-14			
hIR/ 83-7/18-44			
hIR/ 83-7/83-14			

Figure 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00998

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: C07K 14/705, 14/71; G06F 17/50, 19/00, 159:00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN CAS-ON-LINE: keywords
MEDLINE :keywords

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 90/00562 (DEMEYTS) 25 January 1990 See whole document	1-33
P,X	Protein Science, 1997, no. 6, pages 2663-2666 Mckern, NM et al, "Crystallization of the first 3 domains of the human idsulin-lila growth factor -1 receptor See whole document	1-33

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 January 1999	28 JAN 1999
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929	Authorized officer **OI LEE CHAI** Telephone No.: (02) 6283 2482

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 98/00998

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	Nature, vol 394, published 23 July 1998, pages 395-399. Garrett TPJ et al, "Crystal Structure of the first 3 domains of the type -1 insulin-litu growth factor-1 receptor See whole document	1-33

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU 98/00998

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	90/00562	AU	39822/89	DE	68927854	EP	378671
		JP	3501487	US	5227466		

END OF ANNEX